KFAS COVID-19 weekly brief
4th of August 2020
As the COVID-19 continues to impact the wealth and welfare of our society, much remains to be understood about the pandemic and its impact. Hence, the importance of using scientific research, facts and data for a better understanding of the nature of the pandemic, as well as its associated public health issues, to drive policy making in addressing challenges related to healthcare and wellbeing of the population. This newsletter is intended to provide a weekly overview on the latest information on health-related topics surrounding the COVID-19 pandemic, covering five main themes: infection control and prevention, diagnosis and testing, treatment and therapy, training for healthcare professionals and exit strategies. Each edition of the newsletter will cover a specific sub-theme under the five main themes, providing up to date information on available resources, research, data and studies, along with policy recommendations and implications, based on scientific evidence and facts, for decision makers to utilize in developing polices and measures to address the challenges associated with COVID-19 within the healthcare sector.
• New COVID-19 Law Lab to provide vital legal information and support for the global COVID-19 response [WHO]

• Why do asymptomatic COVID-19 cases even happen? [National Geographic]

• Chile wants Covid-19 sniffer dogs to help reopen public spaces [CNN]

• New antibody mix could form ‘very potent’ Covid-19 treatment, say scientists [The Guardian]

• Tencent and Chinese scientists use deep learning to predict fatal COVID-19 cases [Tech Crunch]

• It’s not just dexamethasone: Other steroids may be used to treat critically ill COVID-19 patients, study says [USA Today]

• Coronavirus: The great contact-tracing apps mystery [BBC]

• New Treatment for Covid-19 Shows Promise, but Scientists Urge Caution [NY Times]

• Coronavirus: Cracking the secrets of how bats survive viruses [BBC]

• Can you get coronavirus twice? Doctors are unsure even as anecdotal reports mount. [Washington Post]

• Ebola prepared these countries for coronavirus — but now even they are floundering [Nature]

• Coronavirus: Oxford vaccine triggers immune response [BBC]

• Sweden’s Coronavirus Approach Doesn’t Pay Off for the Economy [Bloomberg]

• Colleges Spent Months Planning For Fall, But A COVID-19 Surge Is Changing Everything [NPR]

• Opinion: It’s ethical to test promising coronavirus vaccines against less-promising ones [PNAS]
Executive Summaries

Infection Control and Prevention:

Epidemiologists and mathematicians project that the widespread wearing of face masks could prevent tens of thousands of deaths by COVID-19. Face covering mandates have shown to decrease the number of overall infections and deaths due to the virus. This section will explore the available data and the recommendations for face-covering mandates in Kuwait.

Diagnosis and Testing:

This section features two infographics that present the latest in diagnostics and testing for easy reading. The first graphic distinguishes tests that identify current infection from tests that identify past infection and discusses some relevant statistics. The second graphic summarizes some of the latest findings and tools in the fields of testing and diagnostics.

Treatment and Therapies:

The SARS-CoV-2 virus is more transmissible than previous coronaviruses and causes a more serious illness than influenza. The SARS-CoV-2 receptor binding domain (RBD) of the spike protein binds to the human angiotensin-converting enzyme 2 (ACE2) receptor as a prelude to viral entry into the cell. Using a naive llama single-domain antibody library and PCR-based maturation, two closely related nanobodies were produced, H11-D4 and H11-H4, that bind RBD (KD of 39 and 12nM, respectively) and block its interaction with ACE2. Single-particle cryogenic Electron Microscopy (cryo-EM) revealed that both nanobodies bind to all three RBDs in the spike trimer. Crystal structures of each nanobody–RBD complex revealed how both nanobodies recognize the same epitope, which partly overlaps with the ACE2 binding surface, explaining the blocking of the RBD–ACE2 interaction. The nanobodies may have application on their own or in additive combinations with other antibodies in the treatment of severely ill COVID-19 patients.

Exit Strategies:

The unprecedented impact of the COVID-19 pandemic exemplifies the critical need for investments in public health research to provide the
evidence base that can protect the lives and health of people and ensure the sustainability and resilience of the health security of a nation. To do that, most countries will have to consider how they are better able to conduct real-time research to develop a strong empirical and analytical evidence base. In the United States (US), the pandemic presented an opportunity to reassess their public health emergency preparedness and response (PHEPR), and in a recent article by the Journal of American Medical Association (JAMA), an outline of what needs to be enhanced and improved was presented. Their findings stemmed from a recent report, published by National Academies of Sciences, Engineering, and Medicine, which provides detailed analyses on the PHEPR and key recommendations on how to transform the infrastructure, funding, and methods used for PHEPR research, which can serve as the foundation for evidence based decision making.
As countries all over the world including Kuwait re-opens from stay-at-home orders, the issue of face-mask mandates for mitigating the spread of COVID-19 has been in question. Both the Centers for Disease Control and Prevention (CDC) and the World Health Organization now recommend cloth masks for the general public. Covering the mouth and nose with filtering materials serves two purposes: personal protection against inhalation of harmful pathogens and particulates, and source control to prevent exposing others to infectious microbes that may be expelled during respiration. It is now clear that both pre-symptomatic and asymptomatic transmission of SARS-CoV-2 are common and may be the critical driver in the spread of the virus.

What evidence do we have that wearing a face mask is effective in slowing down COVID-19 in the community?

There are several strands of epidemiological evidence supporting the use of masks.

1. A recent study published in Health Affairs, compared the COVID-19 growth rate before and after mask mandates in 15 states and the District of Columbia. It found that mask mandates led to a slowdown in daily COVID-19 growth rate. This became more apparent over time. The first five days after a mandate, the daily growth rate slowed by 0.9 percentage-points compared to the daily growth rate at three weeks that had slowed by 2 percentage-points.

2. Another study looked at COVID-19 deaths across 198 countries and found that those with cultural norms or government policies favoring mask-wearing had lower death rates.

3. The CDC cite a case study on COVID-19 prevention in a Missouri hair salon. When two stylists at a Missouri hair salon tested positive for COVID-19, researchers from 4 different institutions worked together to trace contacts, investigate the cases, and publish their findings. One of the stylists developed respiratory symptoms but continued to see clients.

2 Community Use of Face Masks And COVID-19: Evidence From A Natural Experiment of State Mandates in The US, Wei Lyu and George L. Wehby Health Affairs.
3 Christopher T. Leffler Association of country-wide coronavirus mortality with demographics, testing, lockdowns, and public wearing of masks (Update June 15, 2020).
for eight days. The other, who became infected from her co-worker, also developed respiratory symptoms and continued to see clients for four days. The salon in which they worked had a policy requiring both stylists and clients to wear face coverings. Both stylists wore double-layered cloth face coverings or surgical masks when seeing clients. The median appointment time was 15 minutes and ranged from 15 to 45 minutes. More than 98% of clients wore a face covering. When customers were asked whether they had been ill with any respiratory symptoms in the 90 days preceding their appointment, 84% reported that they had not. None of the interviewed customers developed symptoms of illness. Among 48% of customers who volunteered to be tested, all 67 tested negative for SARS-CoV-2. Several family members of one of the stylist’s subsequently developed symptoms and received a diagnosis of COVID-19⁴.

**What do projections model say about the use of face covers?**

1. A model from the University of Washington’s Institute for Health Metrics and Evaluation shows that near-universal wearing of cloth or homemade masks could prevent between 17,742 and 28,030 deaths across the United States before Oct. 1.

   ![Graph showing projected deaths](graph.png)

   **Model Projects Face Masks Could Prevent Thousands Of COVID-19 Deaths**

   The University of Washington’s Institute for Health Metrics and Evaluation’s recent model update shows that near universal wearing of masks from now on can prevent between 17,742 and 28,030 deaths in the U.S. before Oct. 1.

   - **Reported deaths**
   - **Average projected deaths**
   - **Average projected deaths with universal mask-wearing**

   **Source:** NPR: Widespread Use of Face Masks Could Save Tens of Thousands of Lives, Models Project July 3, 2020

⁴ MMWR Article: No Transmission of Symptomatic SARS-CoV-2 After Significant Exposure With Universal Face Mask Use at a Hair Salon – Springfield, Missouri, May 2020 [https://www.cdc.gov/mmwr/volumes/69/wr/mm6928e2.htm?s_cid=mm6928e2_w](https://www.cdc.gov/mmwr/volumes/69/wr/mm6928e2.htm?s_cid=mm6928e2_w)
2. Similarly, a model from the University of Washington’s Institute for Health Metrics and Evaluation shows that near-universal wearing of cloth or homemade masks could also save lives in Kuwait:

3. Another projection developed by researchers at Arizona State University in April showed that 24–65% of projected deaths could be prevented in Washington state in April and May if 80% of people wore cloth or homemade masks in public⁵.

source: https://covid19.healthdata.org/kuwait

⁵ Steffen E. Eikenberry, Marina Mancuso, Enahoro Iboi, Tin Phan, Keenan Eikenberry, Yang Kuang, Eric Kostelich, Abba B. Gumel, To mask or not to mask: Modeling the potential for face mask use by the general public to curtail the COVID-19 pandemic, Infectious Disease Modelling, Volume 5, 2020,
What does the current mask-wearing practices look like around the world and the Middle East?

Key drivers of cases and deaths: Masks
% who self-report they always wear a mask when going out (June 23)

Source: University of Washington “IHME COVID-19 Model Overview”-Bobby Reiner

What should be done?

Globally, health authorities have followed different trajectories in recommendations around the use of face masks by the public. In China, Taiwan, Japan and South Korea, face masks were utilized from the start of the pandemic. Other countries, like The Czech Republic and Thailand, were early adopters in a global shift towards recommending cloth masks. Modelling suggests that population level
compliance with public mask wearing of 70% combined with contact tracing would be critical to halt epidemic growth. Population level uptake of an intervention to benefit the whole population is similar to vaccinations. A common policy response to this problem is to ensure compliance by using laws and regulations, such as widespread state laws in the Unites States which require vaccinations to attend school. The same approach is now being used in many jurisdictions to increase mask wearing compliance, by mandating mask use in a variety of settings (such as public transportation or grocery stores or even at all times outside the home). Early results suggest that these laws are effective at increasing compliance and slowing the spread of COVID-19.

**Recommendations:**

1. Public health officials and Ministry of Health leaders need to ensure that the public understands clearly when and how to wear cloth face coverings properly and continue building the evidence base for their effectiveness.

2. The public needs consistent, clear, and appealing messaging that normalizes community masking.

3. The government should mandate the use of face covering in public spaces especially were social distancing is not possible or in indoor spaces with poor ventilation.

4. If the government does not mandate facemask use, it should be mandated by organizations that provide public-facing services. A “no mask, no service” rule may help enforce the mandate.

5. Not only employees should wear masks, customers must wear masks as well.

6. Such mandates must be accompanied by measures to ensure access to masks, possibly including distribution and rationing mechanisms so that they do not become discriminatory, but remain focused on the public health benefit.

7. It is also important for the Ministry of Health to provide clear guidelines for the production, use and sanitization or re-use of face masks, and consider their distribution as shortages allow. A number of countries have distributed surgical masks (South Korea, Taiwan) from early on, while Japan, Singapore and Belgium are now distributing cloth masks to their entire populations.

8. Clear and implementable guidelines can help increase compliance and bring communities closer to the goal of reducing and ultimately stopping the spread of COVID-19.

In conclusion, as COVID-19 is resurging around the world, broad adoption of cloth face coverings is a civic duty, a small sacrifice reliant on a highly effective low-tech solution that can help turn the tide favorably in the global efforts against COVID-19. “We are not defenseless against COVID-19,” said CDC Director Dr. Robert R. Redfield. “Cloth face coverings are one of the most powerful weapons we have to slow and stop the spread of the virus – particularly when used universally within a community setting.”
Diagnosis and Testing

THE LATEST IN DIAGNOSTICS

THESE 5 INNOVATIONS OFFER TESTING SOLUTIONS

1. SAMPLE POOLING
Combining multiple samples into one test allows for increased testing capacity within the current available laboratory infrastructure and test kits. Pooling samples is recommended for asymptomatic individuals and for those from areas with low levels of prevalence (<5%).

2. WASTEWATER TESTING
Used in many countries to estimate the total number of infections in a community when individual testing is limited. Can also be utilized as an early-warning system to identify outbreaks in communities or facilities, reportedly up to a week before a case is formally identified.

3. ACCURATE RAPID-TESTS
Hailed as the next-generation of COVID-19 diagnostics, these tests hope to enable on-site rapid testing without compromising accuracy and sensitivity. Tests include: antigen tests from 3M and Becton Dickenson, next-generation antibody tests, and instant result molecular-based tests.

4. SNIFF TESTS
Fever checks miss asymptomatic and pre-symptomatic cases but smell tests might not. Recent findings indicate smell tests could be more effective than temperature checks used currently. Countries are beginning to develop smell test kits in response to findings.

5. CRISPR-BASED TESTS
MIT’s Broad Institute scientists are using the gene-editing tool, CRISPR, to develop a test that would deliver results detectable by smartphone in less than an hour and with 90% accuracy. Other CRISPR applications are being developed to test many samples at once.

Please refer to Appendix 1 on page 24 for references
COVID-19

HOW TO TEST FOR:

CURRENT INFECTION

MOLECULAR-BASED RT-PCR
- ACCURACY: 70-90%
  - More likely 70% in community settings
- Performs best: 3 days after symptom onset
- Results in: 4 hrs - 3 days
- Tests for: Viral RNA

ANTIGEN TEST
- ACCURACY: 84%
  - More accurate tests are in development
- Performs best: Days 1-4 of symptom onset
- Results in: 15-30 minutes
- Tests for: Viral Proteins

PREVIOUS INFECTION

ANTIBODY TEST
- ACCURACY: 70-90%
  - As low as 30% if the test is taken too soon
- Performs best: 15-35 days after symptom onset
- Results in: 30 min - 1 hour
- Tests for: Immune response

WHERE YOU GET YOUR RESULTS:

MOLECULAR-BASED RT-PCR
- Tests are processed in diagnostic labs
- At-home saliva and swab kits are in development but still require lab processing

ANTIGEN TEST
- Tests are processed in diagnostic labs
- 3M at-home spit tests are currently in development

ANTIBODY TEST
- At home tests are available but accuracy is questionable and as low as 30%
- The first 8 days of symptom onset

Infographic made by: Lila Almazawa for KFAS EH Response

Please refer to Appendix 1 on page 25 for references
Treatment and Therapy

Treatment in development: Immune therapy -Neutralizing Nanobodies.

The single-positive-strand RNA genome of SARS-CoV-2, like SARS-CoV, encodes four major structural proteins: spike, envelope, membrane and nucleocapsid. The spike protein comprises an N-terminal (S1) subunit, which contains the roughly 200-residue receptor binding domain (RBD)\(^1\), and a C-terminal subunit (S2), which contains the fusion protein (Fig.1a). The RBD of SARS-CoV-2 binds more tightly to the extracellular domain of angiotensin-converting enzyme 2 (ACE2) (Fig.1a) than the homologous SARS-CoV-1 RBD. The higher affinity results from sequence changes in RBD (Fig.1b) and this has been proposed to underlie the higher transmissibility of SARS-CoV-2. Antibodies raised to the spike protein of SARS-CoV-1 can neutralize the virus both in vitro and in vivo, by binding to the RBD and blocking binding to ACE2. Unfortunately, most of these antibodies do not cross-react with the SARS-CoV-2 RBD. The CR3022 antibody derived from a convalescent SARS-CoV-1 patient is cross-reactive to both SARS-CoV-1 and SARS-CoV-2 RBD (reported apparent KD of 6nM)\(^2\). Two studies have reported crystal structures of CR3022 bound to SARS-CoV-2 RBD and show that the target epitope is distant from the ACE2 binding region, which is consistent with the observation that CR3022 does not block RBD binding to ACE2. Another study on CR3022 has reported highly effective SARS-CoV-2 neutralizing activity that appears to arise from destabilization of the spike trimer, a novel mechanism for neutralizing SARS-CoV-2\(^2\). Destabilization of viral proteins by antibodies has been observed for influenza and human immunodeficiency virus.

Mammalian, including human, antibodies generally have two chains (heavy and light), but camels, in addition to two-chain antibodies, also possess a single-heavy-chain antibody variant\(^1\). The antigen-specific variable portion of this single-chain antibody is termed the VHH domain and is commonly referred to as a nanobody (Fig.1c). In addition to compatibility with phage display, nanobodies are small, stable and straightforward to produce. As a result, they serve as alternates to conventional antibodies as diagnostics, imaging agents and structural biology tools. The direct application of nanobodies in oncology and inflammatory diseases is being evaluated, with caplacizumab \(^3\) approved for use. Nanobodies have been developed against SARS-CoV-1 and are currently being developed against SARS-CoV-2, both as research tools and potential therapeutics.

\(^1\) www.nature.com
\(^2\) https://www.tandfonline.com/doi/full/10.1080/22221751.2020.1729069
\(^3\) www.nature.com
The identification and characterization of two high-affinity nanobodies (H11-D4 and H11-H4) to the spike protein of SARS-CoV-2 that block the attachment of spike to ACE2 in vitro was reported\(^1\). Structural characterization of both nanobodies in complex with both full-length spike or with the RBD from SARS-CoV-2 has revealed that both target an epitope immediately adjacent to and slightly overlapping with the ACE2 binding region. Both nanobodies, when fused to immunoglobulin-G (IgG) Fc, neutralized live virus, with H11-H4-Fc showing a particularly high potency (50% neutralization dose (ND\(_{50}\)) of 4–6 nM). H11-H4 also showed additive neutralization with CR3022. The nanobodies may have application on their own or in additive combinations with other antibodies in the treatment of severely ill COVID-19 patients.

Fig. 1: The spike protein of SARS-CoV-2 drives infection.  source: https://www.nature.com/

**a**, Schematic of the spike protein of SARS-CoV-2. The spike protein is composed of S1 and S2 subunits. S1 contains the RBD (highlighted in red). Using the RBD, the trimeric spike molecule binds to ACE2 on human cells (a single ACE2 is shown in blue).

**b**, RBD residues that are shared between SARS-CoV-2 and SARS-CoV-1 are highlighted in cyan (SARS-CoV-2, top) or in light grey text (SARS-CoV-1, bottom). Residues that contact ACE2 are highlighted in red for each sequence. Other sequence differences are in black text, with conservative substitutions indicated by colons (:) underneath. Residues in contact with the H11-H4 nanobody are boxed.

**c**, Camelids have antibodies that are dimers of a single chain. The constant region is in black and the variable region in yellow. When the VHH domain is expressed on its own, it is termed a nanobody. A topology diagram shows that the nanobody is composed of two \(\beta\)-sheets. Three loops—complementarity-determining region 1 (CDR1), CDR2 and CDR3—control antigen binding and are highlighted in purple\(^3\).

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\(^3\) www.nature.com
It is assumed that, during the virus life cycle, the spike trimer exists in an equilibrium between the all ‘down’ configuration and mixed ‘up down’ states. The spike protein can only bind to ACE2 with the RBD in the ‘up’ state and this results in dissociation of the trimer. SARS-CoV-2 spike binds to ACE2 with a 10- to 20-fold higher affinity (KD of ~15 nM) than SARS-CoV-1 spike, a fact that has been proposed to drive its higher transmissibility. Neutralizing antibodies that have been identified so far for SARS-CoV-1 bind to the RBD of the spike protein and many do so by blocking ACE2 binding, but CR3022 operates by a different mechanism. Two nanobodies, H11-H4 and H11-D4 were identified, which differ in sequence at five residues within the CDR3 loop and have shown some subtle differences in properties. Given that the H11-H4 nanobody has the higher affinity for RBD, the discussion focuses on this variant, but, unless explicitly stated, is equally valid for H11-D4.

The researchers have shown that H11-H4 binds with high affinity to RBD, blocks ACE2 binding and neutralize the virus. Their analysis has suggested that H11-H4 would bind to both the ‘all down’ as well as ‘two down one up’ conformations of RBD within the spike. The epitope on SARS-CoV-2 RBD that is recognized by H11-H4 overlaps only to a limited degree with the ACE2 binding region. This region of SARS-CoV-2 RBD has several sequence changes when compared to SARS-CoV-1 RBD (Fig.1b).

The lack of conservation of the H11-H4 epitope between SARS-CoV-1 and SARS-CoV-2 raises the possibility that SARS-CoV-2 variants may emerge that retain ACE2 receptor binding but are no longer recognized by H11-H4 or its relatives. At least some of the plausible escape mutations would alter the position of Phe486, which inserts into a cleft in ACE2, an interaction important to the increased affinity of SARS-CoV-2. The rapid pipeline from naive library screen to maturation and thorough characterization does offer the possibility that new nanobodies could be generated against SARS-CoV-2 viruses that have escaped H11-H4.

The use of convalescent serum has shown clinical promise—to some extent—in patients severely ill with SARS-CoV and most recently SARS-CoV-2; such passive immune therapy has a long history in medicine. The use of laboratory-produced reagents avoids some of the infection risks that arise from use of human serum and can be administered in smaller volumes. The use of antibodies as therapies is well established but nanobodies have now entered clinical trials, with one, caplacizumab, now licensed. The direct injection of a nanobody has also shown promise in a mouse model of cobra venom intoxication. Camelid VHH domains are highly conserved with their human counterparts, and their immunogenicity has been proposed to be low, although humanization strategies are well developed.
To increase the in vivo half-life and enhance avidity, nanobodies can be multimerized by a variety of means. For in vitro binding assays and neutralization experiments, the research team created a dimeric Fc fusion construct. Because the CR3022 antibody recognized a different epitope than H11-H4, the researchers investigated a combination of H11-H4 and CR3022 (CR3022 concentration fixed at 84 nM). Under these assay conditions, evidence was observed for an additive effect. Such additive combinations are a well-known strategy to reduce the propensity of the virus to escape by mutating.

This work establishes that nanobody maturation technology can be deployed to produce a highly neutralizing agent against an emerging viral threat in real time. The approach may be useful in identifying complementary epitopes to those identified by animal immunization approaches. The H11-H4 and H11-D4 nanobodies may find application in a mixed of laboratory-synthesized neutralizing antibodies given for passive immunization of severely ill COVID-19 patients.
Exit Strategies

Strengthening Public Health Emergency Response: Evidence is Key

As countries continue to deal with the implications of the pandemic and reflect on the types of measures and interventions needed to better prepare them for addressing public health emergencies, one issue that has been highlighted is the importance of using scientific evidence to drive policymaking and build a culture of evidence-based decision making. This starts with addressing the limitations and gaps within the national public health infrastructure for gathering the evidence needed, including considering limitations in relation to capacity and investment that is essential to foster the desired change and improvements.

In the United States (US), the pandemic presented an opportunity to reassess their public health emergency preparedness and response (PHEPR), and in a recent article by the Journal of American Medical Association (JAMA), an outline of what needs to be enhanced and improved were presented. Their findings stemmed from a recent report, published by National Academies of Sciences, Engineering, and Medicine, which provides detailed analyses on the PHEPR and key recommendations on how to transform the infrastructure, funding, and methods used for PHEPR research that can serve as the foundation for evidence-based decision making. The main focus of the report was to enhance PHEPR research, and gather robust and credible evidence to advance and enhance PHEPR in the future.

General Findings of the Report from the Evidence-Based Practice for Public Health Emergency Preparedness and Response (2020)

The Centers for Disease Control and Prevention (CDC) in the United States were looking for clear guidance on how to improve PHEPR practices through evidence-based decision making, particularly for practitioners during a public health threat. They were also interested in developing a well-defined methodology that can be used for assessing PHEPR practices. Hence, a committee from the National Academies of Sciences, Engineering, and Medicine completed a comprehensive assessment and evaluation of PHEPR practices, providing recommendations using research to address the current gaps within evidence-based PHRPR practices, as well as how to improve the overall quality of the evidence that is used for decision making.

The report found that, despite the investments made in the past two decades, there are still some major deficiencies that have hampered the country’s ability to respond to public health emergencies, effectively and efficiently. One of these gaps is the lack of a clear and progressive research agenda, along with the funding needed to support the agenda. This has led to sparse, scattered evidence, and data gathered through differing methodologies, in relation to research design, implementation, reporting, synthesis, and translation. Furthermore, the funding has often been sporadic and not always focused on addressing the challenges of public health practitioners. It was also noted that the funding and prioritization of research, during a public health emergency, was fragmented and unorganized amongst the different funding agencies. Furthermore, there was a lack of commitment to ensure that a certain quality of research was maintained, and efforts to ensure a sustainable development of research expertise.

As a result of these findings, the committee recommended that the CDC lead the development of a National PHEPR Science Framework, which should contain defined goals and objectives for improving coordination, integration and alignment between various institutions engaged in PHEPR research. The goal is to ensure that the research funding and efforts are prioritized to address important knowledge gaps, addressing the challenges faced within the PHEPR system. In addition, the framework should emphasize the importance of collaborations and partnerships to enhance PHEPR research, as well as the importance in the translation of research into practice, either through practitioners or policy makers, which can help bridge the gap between research and practice. The committee also noted the significant role of federal level leadership as a part of the framework. Other general areas highlighted in the report:

- Challenges in PHEPR Research

PHEPR systems are quite complex, and during public health emergencies, they contain many moving parts, adding inherent challenges of conducting research, as illustrated by the COVID-19 pandemic. Thus, the complexity of the PHEPR system has resulted in the need for methodological improvements in relation to PHEPR research, ensuring the establishment of clear guidelines for evaluating methods and study designs that should be used for all types of research, including exploratory case studies, randomized trials, and modeling studies. Furthermore, methodologies should exist for the strategic use of mixed research methods to improve the understanding of the findings.
Another area for improvement for PHEPR research is with the source of the evidence, including the collection of experiential evidence during a public health emergency. The Committee noted that the CDC in collaboration with the Federal Emergency Management Agency should convene a panel of experts on the local, regional state and national level to enhance the quality and use of After Action Reports (AAR). These reports are created by public health authorities, and other response organizations, after a public health emergency or crisis, to provide insight into lessons learned and recommendations for future responses. These reports serve as a good basis for research data and can greatly enhance PHEPR research if they are more rigorously structured, reliable, and capable of being analyzed systematically. It is also recommended that AARs be readily available and accessible by establishing a national repository as evidence for lessons learned and best practices for policymakers, researchers and practitioners.

• Capacity Building for PHEPR Researchers and Practitioners\textsuperscript{1,2}

The committee also noted the need to improve and expand the capabilities of both PHEPR researchers and practitioners, including advancing skills to foster an interdisciplinary research workforce. The report also highlighted the need to train practitioners to engage in research evaluations, by providing the necessary technical training, as well as improving peer networking and building sustainable practitioner-researcher partnerships.

• Translation of Research into Practice\textsuperscript{1,2}

It is essential that the research and evidence collected is translated into clear evidence-based practices for public health agencies so that practitioners do not continue to implement ineffective or inappropriate practices. As noted earlier, this is based on the premise that the evidence collected is robust and credible, which will allow researchers and practitioners to collaborate on identifying critical research gaps; thus, funding agencies will also be able to assess how to divert their investments into priority research areas.

• Main Recommendations from the Report\textsuperscript{2}

The Committee provided eight high level recommendations, which, in their perspective would shift and improve PHEPR towards a more structure and reliable evidence based practice, by transforming the infrastructure, funding and research methodology. The eight main recommendations are as follows:

1. The CDC should appoint a Public Health Emergency Preparedness and Response (PHEPR) Evidence-Based Guidelines Group, an independent group that will be responsible for developing methodological and
transparent evidence-based guidelines for PHEPR practices, taking into consideration the advances in quantitative, qualitative, and experiential evidence.

2. The CDC should establish the infrastructure, as well as policies and procedures, for conducting and updating evidence reviews, along with guidelines for practice.

3. The CDC should work with other relevant funding agencies, including public health institutions, academic and researcher institutions, as well as others to develop a National Public Health Emergency Preparedness and Response (PHEPR) Science Framework, which should:
   
a. Enhance the integration and alignment for PHEPR research
   
b. Improve research competencies to support PHEPR, by recognizing and supporting PHEPR science as a discipline, under the broader field of public health research
   
c. Develop a PHEPR research agenda that involves not only the traditional epidemiological research, but also involves advancing research in disciplines, such as social science, implementation science, complex interventions, operations, systems, quality improvement, as well as others.
   
d. Promote and support collaborations between PHEPR practitioners and researchers, to ensure the translation of PHEPR research to practice.
   
e. Ensure the dissemination and implementation of PHEPR research through the development of sustainable strategies.

4. It is recommended that the CDC, in collaboration with other relevant funding agencies, ensure funding is provided to support a National PHEPR Science Framework, and to support the infrastructure necessary for better quality PHEPR research. The infrastructure should include:
   
a. Funding for practice based and investigator driven research
   
b. Support for collaborative research with partners from other institutions, such as academic institutions, hospital systems, etc.
   
c. Development of a rapid research funding mechanism to support studies related to the implementation of PHEPR practices during a public health emergency or crisis
d. Enhanced mechanisms to promote and support routine collection of data, through a standard and efficient manner, with minimal disruption of services.

5. There should be an effort to improve the conduct and reporting associated with the PHEPR Research, especially in relation to the effectiveness and implementation of PHEPR practices. This will involve establishing guidelines for evaluations and reporting.

6. Convene a panel of experts from federal agencies to improve the quality and utility of AARs. The goal is to develop standards and expectations for the information reported in AARs through process development, as well as develop a national repository for these reports³.

7. The CDC should focus and support capacity building and technical assistance programs for PHEPR research and practitioners, by working with professional and academic institutions to build a research training infrastructure, which should include career development grants. Training grants should foster PHEPR evidence based research, through the use of appropriate research methodology and designs. There should also be some effort on developing a training and certification program for CDC project officers and state officials, familiarizing them with evidence-based decision making practices.

8. Translate, disseminate and implement PHEPHR research into practice through a coordinated effort from the evidence based guidelines that result from Recommendation #1.

Policy Implications and Recommendations

The unprecedented impact of the COVID-19 pandemic exemplifies the critical need for investments in public health research to provide the evidence base that can protect the lives and health of people and ensure the sustainability and resilience of the health security of a nation. Although not all countries have the same infrastructure for addressing public health emergencies, the COVID-19 pandemic has presented an opportune time to reevaluate and reassess the current measures and infrastructure in place. At the core of establishing a more resilient and effective public health emergency response, is creating and building practices based on scientific evidence. To do that, most countries will have to consider how they are better able to conduct real-time research to develop a strong empirical and analytical evidence base. This will not only require investment, but the development of a solid research agenda, defining methodologies to ensure robust research design and conduct, as well as the training of researchers and practitioners in the public health realm. Understanding the limitations

³ While maintaining privacy issues in relation to the data and information collected from use in legal proceedings.
of data availability, as well as collection and storage, should also be reflected on, and considerations for how these can be improved should be a part of the new measures implemented.

National PHEPR Science Framework. Source: National Academy of Sciences (Reference 2)
Sources for Infographic at page 12:


Sources for Infographic at page 13:


