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Health and Medicine Division

***Disclaimer:** This list of research topics was prepared by Health and Medicine Division (HMD) staff as an informal record of issues that were discussed during the public session of the Standing Committee on Emerging Infectious Diseases and 21<sup>st</sup> Century Health Threats meeting, held on March 11, 2020. This document was prepared for information purposes only. It has not been peer reviewed and should not be cited or quoted, as the views expressed do not necessarily reflect the views of the National Academies of Sciences, Engineering, and Medicine's Standing Committee on Emerging Infectious Diseases and 21<sup>st</sup> Century Health Threats.*

**Standing Committee on Emerging Infectious Diseases and 21<sup>st</sup> Century Health Threats**

Meeting #1: March 11, 2020

**Research Topics Discussed**

The following research topics were discussed at the first meeting of the Standing Committee on Emerging Infectious Diseases and 21<sup>st</sup> Century Health Threats with the sponsors (Office of Science and Technology Policy and the Office of the Assistant Secretary for Preparedness and Response). Please note this is a first cut at many of the very important questions regarding the current COVID-19 outbreak, if you would like to submit additional questions or topics, please submit them to [SCEID@nas.edu](mailto:SCEID@nas.edu).

**Virus Characteristics**

- *Virus genetics, origin, and evolution*
  - Examples of short-term research needs
    - Real-time tracking of whole genomes and a mechanism for coordinating the rapid dissemination of that information to inform the development of diagnostics and therapeutics and to track variations of the virus over time.
    - Access to geographic and temporal diverse sample sets to understand geographic distribution and genomic differences, and determine whether there is more than one strain in circulation. Multi-lateral agreements such as the Nagoya Protocol could be leveraged.
  - Examples of long-term research needs
    - Evidence that livestock could be infected (e.g., field surveillance, genetic sequencing, receptor binding) and serve as a reservoir after the epidemic appears to be over.
      - Evidence of whether farmers are infected, and whether farmers could have played a role in the origin.
      - Surveillance of mixed wildlife- livestock farms for SARS-CoV-2 and other coronaviruses in Southeast Asia.
      - Experimental infections to test host range for this pathogen.
- *Transmission, incubation, and environmental stability*
  - Examples of short-term research needs

- Range of incubation periods for the disease in humans (and how this varies across age and health status) and how long individuals are contagious, even after recovery.
- Prevalence of asymptomatic shedding and transmission (e.g., particularly children).
- Seasonality of transmission.
- Physical science of the coronavirus (e.g., charge distribution, adhesion to hydrophilic/phobic surfaces, environmental survival to inform decontamination efforts for affected areas and provide information about viral shedding).
- Persistence and stability on a multitude of substrates and sources (e.g., nasal discharge, sputum, urine, fecal matter, blood).
- Persistence of virus on surfaces of different materials (e.g., copper, stainless steel, plastic).
- *Risk factors*
  - Examples of short-term research needs
    - Data on potential risks factors
      - Smoking, pre-existing pulmonary disease
      - Co-infections (determine whether co-existing respiratory/viral infections make the virus more transmissible or virulent) and other co-morbidities
      - Neonates and pregnant women
      - Socio-economic and behavioral factors to understand the economic impact of the virus and whether there were differences.

## **Diagnostics and Surveillance**

- *Systematic, holistic approach to diagnostics (from the public health surveillance perspective to being able to predict clinical outcomes)*
  - Examples of short-term research needs
    - Evaluate how widespread current exposure is to be able to make immediate policy recommendations on mitigation measures. Denominators for testing and a mechanism for rapidly sharing that information, including demographics, to the extent possible. Sampling methods to determine asymptomatic disease (e.g., use of serosurveys (such as convalescent samples) and early detection of disease (e.g., use of screening of neutralizing antibodies such as ELISAs),
    - Efforts to increase capacity on existing diagnostic platforms and tap into existing surveillance platforms.
    - Recruitment, support, and coordination of local expertise and capacity (public, private—commercial, and non-profit, including academic), including legal, ethical, communications, and operational issues.
    - National guidance and guidelines about best practices to states (e.g., how states might leverage universities and private laboratories for testing purposes, communications to public health officials and the public).
    - Development of a point-of-care test (like a rapid influenza test) and rapid bed-side tests, recognizing the tradeoffs between speed, accessibility, and accuracy.
    - Rapid design and execution of targeted surveillance experiments calling for all potential testers using PCR in a defined area to start testing and report to a specific entity. These experiments could aid in collecting longitudinal samples, which are critical to understanding the impact of ad hoc local interventions (which also need to be recorded).
    - Separation of assay development issues from instruments, and the role of the private sector to help quickly migrate assays onto those devices.

- Establish efforts to track the evolution of the virus (i.e., genetic drift or mutations) and avoid locking into specific reagents and surveillance/detection schemes.
- Latency issues and when there is sufficient viral load to detect the pathogen, and understanding of what is needed in terms of biological and environmental sampling.
- Use of diagnostics such as host response markers (e.g., cytokines) to detect early disease or predict severe disease progression, which would be important to understanding best clinical practice and efficacy of therapeutic interventions.
- Policies and protocols for screening and testing.
- Policies to mitigate the effects on supplies associated with mass testing, including swabs and reagents.
- Examples of long-term research needs
  - Technology roadmap for diagnostics.
  - Barriers to developing and scaling up new diagnostic tests (e.g., market forces), how future coalition and accelerator models (e.g., Coalition for Epidemic Preparedness Innovations) could provide critical funding for diagnostics, and opportunities for a streamlined regulatory environment.
  - New platforms and technology (e.g., CRISPR) to improve response times and employ more holistic approaches to COVID-19 and future diseases.
  - Coupling genomics and diagnostic testing on a large scale.
  - Enhance capabilities for rapid sequencing and bioinformatics to target regions of the genome that will allow specificity for a particular variant.
  - Enhance capacity (people, technology, data) for sequencing with advanced analytics for unknown pathogens, and explore capabilities for distinguishing naturally-occurring pathogens from intentional.
  - One Health surveillance of humans and potential sources of future spillover or ongoing exposure for this organism and future pathogens, including both evolutionary hosts (e.g., bats) and transmission hosts (e.g., heavily trafficked and farmed wildlife and domestic food and companion species), inclusive of environmental, demographic, and occupational risk factors.

## Medical Care

- *Surge capacity and nursing homes*
  - Examples of short-term research needs
    - Resources to support skilled nursing facilities and long term care facilities.
    - Mobilization of surge medical staff to address shortages in overwhelmed communities
- *Efforts to inform allocation of scarce resources*
  - Examples of short-term research needs
    - Age-adjusted mortality data for Acute Respiratory Distress Syndrome (ARDS) with/without other organ failure – particularly for viral etiologies
    - Extracorporeal membrane oxygenation (ECMO) outcomes data of COVID-19 patients; and,
    - Outcomes data for COVID-19 after mechanical ventilation adjusted for age.
    - Knowledge of the frequency, manifestations, and course of extrapulmonary manifestations of COVID-19, including, but not limited to, possible cardiomyopathy and cardiac arrest.

- Application of regulatory standards (e.g., EUA, CLIA) and ability to adapt care to crisis standards of care level.
- *Personal Protective Equipment*
  - Example of short-term research needs
    - Approaches for encouraging and facilitating the production of elastomeric respirators, which can save thousands of N95 masks.
- *Alternative methods to advise on disease management*
  - Examples of short-term research needs
    - Best telemedicine practices, barriers and facilitators, and specific actions to remove/expand them within and across state boundaries.
    - Guidance on the simple things people can do at home to take care of sick people and manage disease.
    - Oral medications that might potentially work.
  - Example of long-term research needs
    - Use of AI in real-time health care delivery to evaluate interventions, risk factors, and outcomes in a way that could not be done manually.
- *Processes of care*
  - Example of short-term research needs
    - Best practices and critical challenges and innovative solutions and technologies in hospital flow and organization, workforce protection, workforce allocation, community-based support resources, payment, and supply chain management to enhance capacity, efficiency, and outcomes.

## **Non-Pharmaceutical Interventions**

- *Effectiveness*
  - Examples of short-term research needs
    - Guidance on ways to scale up NPIs in a more coordinated way (e.g., establish funding, infrastructure and authorities to support real time, authoritative (qualified participants) collaboration with all states to gain consensus on consistent guidance and to mobilize resources to geographic areas where critical shortfalls are identified) to give us time to enhance our health care delivery system capacity to respond to an increase in cases.
    - Rapid design and execution of experiments to examine and compare NPIs currently being implemented. DHS Centers for Excellence could potentially be leveraged to conduct these experiments.
    - Rapid assessment of the likely efficacy of school closures, travel bans, bans on mass gatherings of various sizes, and other social distancing approaches.
- *Equity and barriers to compliance*
  - Example of short-term research needs
    - Methods to control the spread in communities, barriers to compliance and how these vary among different populations..
  - Examples of long-term research needs
    - Models of potential interventions to predict costs and benefits that take account of such factors as race, income, disability, age, geographic location, immigration status, housing status, employment status, and health insurance status.
    - Policy changes necessary to enable the compliance of individuals with limited resources and the underserved with NPIs. Research on why people fail to comply

with public health advice, even if they want to do so (e.g., social or financial costs may be too high).

- Research on the economic impact of this or any pandemic. This would include identifying policy and programmatic alternatives that lessen/mitigate risks to critical government services, food distribution and supplies, access to critical household supplies, and access to health diagnoses, treatment, and needed care, regardless of ability to pay.

## **Vaccines & Therapeutics**

- *Research and development and evaluation efforts*
  - Examples of short-term research needs
    - Evaluate/investigate effectiveness of drugs being developed and tried to treat COVID-19 patients.
      - Clinical and bench trials to investigate less common viral inhibitors against COVID-19 such as naproxen, clarithromycin, and minocycline that may exert effects on viral replication.
    - Methods to evaluate potential complication of Antibody-Dependent Enhancement (ADE) in vaccine recipients.
    - From a clinical development perspective, explore use of best animal models and their predictive value for a human vaccine.
    - Capabilities to discover a therapeutic (not vaccine) for the disease, and clinical effectiveness studies to discover therapeutics, to include antiviral agents.
    - Alternative models to aid decision makers in determining how to prioritize and distribute scarce, newly proven therapeutics as production ramps up. This could include identifying approaches for expanding production capacity to ensure equitable and timely distribution to populations in need.
  - Example of long-term research needs
    - Efforts targeted at a universal coronavirus vaccine.

## **Risk Communication**

- *Communicating with high-risk populations*
  - Examples of short-term research needs
    - Modes of communicating with target high-risk populations (elderly, health care workers).
    - Risk communication and guidelines that are easy to understand and follow (include targeting at risk populations' families too).
    - Communication that indicates potential risk of disease to all population groups.
- *Clarify community measures*
  - Example of short-term research needs
    - Clarify misunderstanding around containment and mitigation.

## **Equity Considerations**

- *Problems of inequity*
  - Examples of short-term research needs
    - Action plan to mitigate gaps and problems of inequity in the Nation's public health capability, capacity, and funding to ensure all citizens in need are supported and can access information, surveillance, and treatment.

- Measures to reach marginalized and disadvantaged populations.
- Data systems and research priorities and agendas incorporate attention to the needs and circumstances of disadvantaged populations and underrepresented minorities.
- Understand and mitigate threats to incarcerated people from COVID-19, assuring access to information, prevention, diagnosis, and treatment.
- Understand coverage policies (barriers and opportunities) related to testing, treatment, and care

### **Information Sharing & Inter-sectoral Collaboration**

- *Data standards and nomenclature*
  - Examples of short-term research needs
    - Methods for coordinating data-gathering with standardized nomenclature.
    - Consistent platform for sharing response information among planners, providers, and others.
    - Understand and mitigate barriers to information-sharing.
- *Governmental public health*
  - Example of short-term research needs
    - Determine how to recruit, support, and coordinate local (non-Federal) expertise and capacity relevant to public health emergency response (public, private—commercial and non-profit, including academic).
  - Examples of long-term research needs
    - Better integration of federal/state/local public health surveillance systems.
    - Value of investments in baseline public health response infrastructure preparedness capacity and capability.