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2020-04-11/12 DAILY UNM GLOBAL HEALTH COVID-19 BRIEFING

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DAILY UNM GLOBAL HEALTH COVID-19 BRIEFING

April 11-12, 2020

Executive Summary

No NM church gatherings. NM a testing champ. Consolidation of elderly care. NM case update. 50-state disaster. Ventilator haggling. Economy reopening planning. PPE decontamination. Hospital ward contamination. Prolonged return to normal. FEMA projections. WHO tracking app. China SEIR model. Hubei epi. Mortality best measure. Covid-19 wave 2. Public should wear masks. Civil liberties. Safe grocery shopping. School closure impact. CDC caretaker guidelines. Psychiatric mobilization. Keep newborns with mom. C-section protocol. Italian obstetrics. Pediatric cardiac catherization. Chinese anesthesiology consensus. Cancer guidelines. Neuro-oncologic Tx. Radiology algorithm. Lung ultrasonography. ARF care. VTE common and predictable. Liver transplantation. Auto-immune treatments. Extracorporeal kidney involvement. Nutrition support. GI endoscopy. No stay-at-home for stroke. Intensive care collaboration. Supine swab collection. Lab tests for severity. Testing assay performance. False negative RT-PCR tests. IgM and IgG serum tests. FDA convalescent plasma. Blood purification device approval. Erythropoietin treatment. Tissue plasminogen activator. ECMO. Lopinavir/ritonavir study results. Immunotherapy review. Vaccine development. Hydroxychloroquine review. Candidates from in silico/virtual screening. Traditional Indian therapies. US trials update. Pathways and risk factors for death. ACE2 polymorphism. Severity in children. Lung tissue replication. Phylogenetic tracing. Text mining dataset. Risk by blood type.

NM Highlights

- NM bans mass gatherings in houses of worship April 11
 Public health order banning mass gatherings has been amended to include houses of worship.
- In the Mountain West, Utah and New Mexico lead in coronavirus testing

 NM is ranked 8th in the nation and second in the Mountain West at 1,295 tests per 100,000. NY leads nation at 2,130.
- <u>Canyon Transitional Rehabilitation Center in Albuquerque to take elderly COVID-19 patients</u>

 NM officials say the operator of a 73-bed skilled nursing rehabilitation center in Albuquerque NE Heights plans to convert it into a facility that will provide care for elderly. Non-infected to be relocated.
- NM case update

State health officials have announced today 74 additional cases and 6 deaths, with 80 currently hospitalized. Cumulative total of 1,245 positive tests, 26 deaths, 295 recoveries.

US Highlights

- Presidential disaster declaration for all 50 states
 Wyoming was the final state to have a FEMA disaster declaration.
- NY outbids other states for ventilators. Supply and demand gaps in 22 states

 Arkansas thought it had secured ventilators, then deal vanished as NY doubled price and paid cash. Current inventory and additional sought ventilator numbers presented for 22 states. OR, WA, CA offered up spare units for use by other states.
- <u>U.S. States prepare test-and-trace programs to reopen their economies</u>

 MA, UT, ND are among states working on strategies to safely lift social-distancing measures that have shuttered much of the U.S. economy. They have launched new efforts to contain Covid-19, laying plans to test aggressively and hire thousands of

Economics, Workforce, Supply Chain, PPE Highlights

UNM researchers devise process for decontaminating PPE

A team of researchers from UNM developed a process to safely collect, store, and sterilize PPE, including N95 respirators for reuse by HCP. The decontamination process uses hydrogen peroxide vapor and has a capacity to sterilize 1000-3000 N95s per day. A manuscript describing the process has been posted on medRxiv and will be available early next week.

Disinfection of N95 respirators by hydrogen peroxide vapor proposed

Reuse of N95 respirator was proposed by CDC but it carries a risk of contamination and infection to heath care workers. Disinfection of N95 respirator may provide an alternative option if it is necessary to reuse respirators. Disinfection of disposable PPE was attempted whenever the supply was tight during pandemic influenza A and COVID-19. Still unclear to what extent reuse of disposable respirators can be reprocessed for appropriate fit.

• Aerosol and surface distribution of severe acute respiratory syndrome coronavirus 2 in hospital wards

Virus was found to be widely distributed on floors, computer mice, trash cans, and sickbed handrails and was detected in the air at about 4 m from patients at a hospital in Wuhan, China. The authors highly recommend disinfection of shoe soles before walking out of wards containing COVID-19 patients.

• Coronavirus economy plans are clear: No return to normal in 2020

The reports discussed in this Vox article outline various approaches to implementing the surveillance necessary to relax social distancing, ranging from automated smartphone tracking systems to massive and persistent testing systems. Regardless of the plan, the result is far from a return to normal. Without a vaccine, it is likely that any effective effort to relax social distancing will be a prolonged and incremental process, paired with enhanced surveillance and testing mechanisms.

Epidemiology Highlights

FEMA COVID-19 data & analytics task force projection models, 3/31/20

The Steady State & 30 Day shelter- in place scenario (followed by steady-state mitigation measures) estimates the total national ventilator needs to peak at Day 150 (~120k units). This rebound peak is anticipated if mitigation measures are relaxed. According to this scenario, there will be 160M infected, leading to 105M cases; 4.2M (2.6%) will require hospitalization and 720k (0.45%) ICU, resulting in 200k (0.12%) deaths (170k aged 65 or older).

• WHO Go.Data app and online course to facilitate outbreak investigation

App supports timely epidemiological data capture. Multi-language, open source, works online and offline, and supports field data collection, contact tracing, and visualization of chains of transmission.

Prediction of the epidemics trend of COVID-19 in China under public health interventions

A dynamic SEIR (Susceptible-Exposed-Infectious-Removed) model was effective in predicting the COVID-19 epidemic peaks and sizes in China. The implementation of control measures on January 23 2020 was indispensable in reducing the eventual COVID-19 epidemic size.

More severe cases and poorer outcomes in Hubei (epicenter) vs outside Hubei

A Nationwide Analysis of data from China suggest more severe cases and poorer outcomes for COVID-19 patients treated in Hubei (China). Delays in hospitalization after symptom onset might explain differences. This suggests the importance of preserving hospital resources. Future studies to determine the impact of delaying hospitalization are warranted.

CDC reports deaths nationwide are increasing. Mortality rate increased from 4% in week 13 to 6.9% in week 14.

• Epidemiology focus on COVID-19 mortality instead of other parameters

Instead of relying principally on the ratio of deaths to infections — known as the case fatality rate — researchers are looking at the daily deaths attributed to COVID-19 to monitor the impact of the disease and to guide responses. Because of delays in widespread population testing in many countries, and the virus's ability to spread without symptoms, estimates of the

number of total infections remain problematic.

• Beware of the second wave of COVID-19 if restrictions prematurely relaxed

Researcher have modelled the potential adverse consequences of premature relaxation of interventions, and found that such a decision might lead to transmissibility (R naught) exceeding 1 again—ie, a second wave of infections. The finding is critical to governments globally, because it warns against premature relaxation of strict interventions.

Healthcare Policy Recommendations

The precautionary principle: Wear masks even if the evidence is controversial

The search for perfect evidence may be the enemy of good policy. Masks are simple, cheap, and potentially effective. Authors propose that, masks worn at home (when people show symptoms) and outside the home in situations where meeting others is likely (for example, shopping, public transport), could reduce transmission with a relatively small impact on social and economic life. Some of the evidence reviewed is about transmission using medical grade masks; more work is needed to clarify the effectiveness of homemade masks.

Balancing public health restrictions and civil liberties

NEJM legal perspective: widespread restrictions on movement for so many people are both more and less restrictive than many previous public health efforts around public health threats. They argue that we need to safeguard civil liberties and that governments ensure that vulnerable groups are not targeted by restrictions. Gradual relaxation of testing restrictions will be necessary but should be based on assessing individual risk which can only be accomplished by widespread testing. Disease Control, Civil Liberties, and Mass Testing - Calibrating Restrictions during the Covid-19 Pandemic.

• Recommendations on grocery shopping during COVID-19

Multiple questions are answered on safely shopping. Wearing gloves when shopping may not help much because gloves, like hands can become contaminated. Frequent handwashing is most important protection. Limiting trips to the store and increasing home delivery could be helpful.

School closure alone would prevent only 2-4% of deaths: a rapid systematic review

Recent modelling studies of COVID-19 predict that school closures alone would prevent only 2-4% of deaths, much less than other social distancing interventions. Policy makers need to be aware of the equivocal evidence when considering school closures for COVID-19, and that combinations of social distancing measures should be considered. If restrictive social distancing policies are implemented for long periods, consider other social distancing interventions within schools.

CDC issued guidelines for caretakers of COVID-19 patients staying at home

Guidelines include recommendations for keeping patient as separate from other family members as possible and checking frequently for signs of worsening condition.

A psychiatric mobilization needed to help combat COVID-19

In this opinion piece, leading psychiatric researchers propose mounting widespread telemedicine campaigns to address the increasing anxiety and mental health crisis caused by COVID-19. They also suggest that psychiatrists help recruit patients for COVID-19 clinical trials, work on repurposing psychiatric drugs and offer their clinical skills as the needs for more clinicians increases.

Practice Guidelines

<u>Do not separate newborns from contagious mothers</u>

Breastfeed Med article argues separation may not prevent infection, disrupts newborn physiology, stresses mothers, and disrupts immune protection. No evidence separation improves outcomes. WHO and CDC guidelines differ.

• Prototype protocol for Cesarean delivery of COVID-19 patients

The protocol was designed to improve staff readiness, minimize risks and streamline care processes for this unique group of patients. The protocol is adaptable to specific local resources and limitations of individual labor and delivery units. Operating

Room Guide for Confirmed or Suspected COVID-19 Pregnant Patients Requiring Cesarean Delivery.

• <u>Italy's experience with managing the obstetric services during COVID-19</u> Italy's Obstetrics Task Force recommendations for the management of pregnant women.

Pediatric and congenital cardiac catheterization during the COVID-19 pandemic

Guidance and recommendations are provided on the preservation and repurposing of resources to help pediatric cardiac programs develop strategies for patient care during this unprecedented crisis.

• Chinese Society of Anesthesiology consensus: Anesthetic management of cardiac surgical patients

Patients who undergo cardiovascular surgery necessitate extremely high demands from anesthesia personnel and face high risks of mortality and morbidity. Anesthesia management guidelines provided for cardiovascular surgery along with the prevention and control of COVID-19. Guidelines include: preoperative evaluation and prep, anesthetic prep, intraoperative management, anesthetic management, and postoperative care.

• Recommendation for management of cancer surgery cases

The Society of Surgical Oncology (SSO) asked each of the SSO Disease Site Work Group Chairs and Vice Chairs provide their recommendations for managing care in their specialties, assuming a 3- to 6-month delay in care.

Cancer specific guidelines

The recommendations and possible actions are described that should be considered by patients, their caregivers and families, physician, nurses, managers and staff of medical centers involved in cancer diagnosis and treatment. To goals: 1) limiting the exposure of cancer patients to medical environments and 2) modifying the treatment modalities in a manner that reduces the probability of myelosuppression

• Guidelines on management of patients with neuro-oncologic disease

Guidance for neuro-oncology practitioners from the AANS/CNS Tumor Section and Society for Neuro-Oncology. Framework is provided for institutions and governments to help adjudicate treatment allocations to patients with neuro-oncologic disease.

• Integrated radiologic algorithm for COVID-19 Pandemic

On the basis of scientific data, knowledge in thoracic radiology, and their Institutional experience with COVID-19, the authors drew and adapted an integrated radiologic algorithm based on the first 702 cases of patients in Italy who referred to dedicated COVID-19 radiology protocol after first-level clinical triage in a dedicated emergency unit.

• Lung ultrasonography advantages for management of COVID-19

"Based upon our experience, we consider that lung ultrasonography has major utility for management of COVID-19 with respiratory involvement due to its safety, repeatability, absence of radiation, low cost and point of care use; chest CT may be reserved for cases where lung ultrasonography is not sufficient to answer the clinical question."

A consensus for non-ICU ARF SARS-CoV-2 emergency in Italy

Italian respiratory scientific societies propose an early consensus statement for emergency management of non-ICU ARF SARS-CoV-2. It represents the expert opinion of pulmonologists directly involved in the first line of assistance. The Consensus identified two urgent areas for action: a) management, and b) organization

• High prevalence of venous thromboembolism (VTE) -- high D-dimer predicts bad outcomes

Incidence of VTE in severe pneumonia COVID-19 patients was 25% (20/81), of which 8 patients with VTE events died. VTE group was different from non-VTE group in age, lymphocytes count, activated partial thromboplastin time (APTT), D-dimer. D-dimer cut-off of >1.5 μ g/mL predicted VTE with sensitivity of 85.0%, and specificity of 88.5%, and negative predictive value (NPV) of 94.7%.

Management of patients after liver transplantation

The authors reviewed the clinical aspects of 2019-nCoV infection, characteristics of liver transplant recipients, immunosuppressant usage, and potential drug interactions to provide recommendations to clinical staff managing liver transplant recipients during the COVID-19 epidemic.

• Patients with cutaneous auto-immune conditions can continue treatment unless COVID positive

Immunosuppressed patients are not at an increased risk of severe manifestations of COVID-19 compared with the general population. Experts on immune-mediated disease suggest continuation of treatment during the outbreak to prevent disease flares that could otherwise increase healthcare use and patient burden. Experts say immunosuppressive/biologic therapy can be discontinued/postponed if a patient contracts COVID-19, but it should a shared decision on a case-by-case basis.

• Kidney involvement in COVID-19 and rationale for extracorporeal therapies

The prevalence of direct kidney involvement in novel coronavirus disease is low, but such involvement is a marker of multiple organ dysfunction and severe disease. The authors explore potential pathways of kidney damage and discuss the rationale for extracorporeal support with various blood purification strategies in patients who are critically ill.

Nutrition support protocol proposed by Italian experts

A pragmatic protocol for the delivery of nutrition therapy in pre-ICU patients with COVID-19 is published. Protocol was devised by a multidisciplinary team of experts working in Lombardy, Italy, which is the center of the Italian COVID-19 crisis.

• Updated review of GI endoscopy guidelines for procedures, PPE use, etc.

All national and international societies recommend the use of gloves, mask, goggles/face shield, gown, and hairnet during all procedures. N95 or FFP2/3 masks and double gloves were recommended in suspected or confirmed cases. All societies recommend following current standardized reprocessing procedures for equipment. Nearly all societies recommend postponing elective and non-urgent procedures. Most societies recommend screening patients for symptoms prior to procedure. Other recommendations include training for PPE donning and removing and self-surveillance of signs/symptoms by health care workers.

• Stay safe at home with stroke symptoms not safe

Keep a high attention on stroke as an emergency condition. To remain at home with stroke symptoms does not mean to "stay safe at home".

• Intensive care recommendations: collaboration enhances survival of critically ill patients

The pandemic associated challenges include rapid diagnosis and isolation, clinical management and prevention for both COVID-19 and other patients. ICU stakeholders must prepare for increase in critical care bed capacity. Inadequate ICU resources will require critical care triage. Collaboration at the local, regional, national, and international level offers the best chance of survival for the critically ill.

Testing

• Innovative supine position and face screen method for collecting nasopharyngeal swabs

Initially, the nasopharyngeal swabs were collected by sitting position method. The study employed supine position and protective face screen method. The latter method provides better comfort of patients, low exposure risk for operators, in addition to reducing false negative result to some extent, which may help reduce false recurrence of discharged patients. [Clinical application effect of modified nasopharyngeal swab sampling for 2019 novel coronavirus nucleic acid detection].

• Lab tests predictive of severe vs. non-severe outcomes

Changsha China study: compared with the non-severe group (n=131), the severe group (n=30) showed statistical significance in older age, hypertension, bilateral lung plaque shadow, decrease in lymphocyte count, increase in C-reactive protein (CRP), aspartate aminotransferase (AST), lactate dehydrogenase, and creatine kinase.

• Some SARS-CoV-2 detection assays are more sensitive than others

Researchers evaluated assays using 7 different primer/probe sets and one assay kit. They found that the most sensitive assays were those that used the E-gene primer/probe set described by Corman et al. All assays tested were found to be highly specific for SARS-CoV-2, with no cross-reactivity with other respiratory viruses observed in our analyses regardless of the primer/probe set or kit used.

• Could false negative and recurrence be prolonged nucleic acid conversion?

About 21.4% of patients had a "turn positive" of nucleic acid detection by RT-PCR test for SARS-CoV-2 after two consecutive negative results. This appears to be related to the false negative of RT-PCR test and prolonged nucleic acid conversion. False-negative of RT-PCR and prolonged nucleic acid conversion in COVID-19: Rather than recurrence.

Detection of serum IgM and IgG for COVID-19 diagnosis

ELISA for specific IgM and IgG antibodies, has a high-throughput advantage, and avoids false-negative cases that occur with the RT-PCR method. Methods are simple, cheap, require a small amount of serum, and could be good for wide application in seroepidemiological monitoring.

Promising Drugs, Vaccines, Therapies, Clinical Trials

FDA Recommendations for Investigational COVID-19 Convalescent Plasma

FDA has issued guidance to health care providers and investigators on the administration and study of investigational convalescent plasma collected from individuals who have recovered from COVID-19.

FDA authorizes blood purification device to treat COVID-19

FDA issued an emergency use authorization for a blood purification system to treat adult patients with COVID-19 admitted to the ICU with confirmed or imminent respiratory failure.

• Case report of recombinant human Erythropoietin administration saving 80-yo critically ill male

Patient was given antiviral treatments, blood transfusion, plus 4000 IU recombinant human Erythropoietin(rhEPO) due to his severe anemia. Anemia and lymphocytopenia resolved quickly, and he recovered in 7 days.

Potential treatment of COVID-19 using Tissue Plasminogen Activator (tPA)

Severe COVID-19 is characterized with coagulopathy. 71.4% of mortalities due to COVID-19 meet ISTH criteria for disseminated intravascular coagulation, with only 0.6% survivors meeting these criteria. Evidence in both animal models and humans suggest that fibrinolytic therapy in acute lung injury and ARDS improves survival.

COVID-19 case successfully treated using extracorporeal membrane oxygenation (ECMO)

In this case report early ECMO dramatically helped recovery of severely ill patient.

Evidence of effectiveness of lopinavir/ritonavir combined with pneumonia-associated adjuvant drugs

One retrospective study (N=47 hospitalized patients with COVID-19) showed that compared with the treatment of pneumonia-associated adjuvant drugs alone, the combination treatment with LPV/r and adjuvant drugs has a more evident therapeutic effect in lowering the body temperature and restoring normal physiological mechanisms with no evident toxic and side effects.

• A systematic review of immunotherapy for COVID-19

The review shoed that although no serious research has been done on this subject at the time of writing this article, similar studies on the related viruses showed notable results. Thus, immunotherapy for COVID-19 can also be a suitable option.

• A review on COVID-19 vaccine development

A review of COVID-19 vaccine candidates and vaccine development platforms is provided.

No drug should be assumed to be efficacious: Oxford review on Chloroquine and HCQ

No intervention should be assumed to be efficacious for COVID-19. Even drugs initially supported by evidence of effectiveness may later prove to be more harmful than beneficial. Too many medicines have been withdrawn because of adverse reactions after showing clinical promise. We need better, properly powered, randomized controlled trials of chloroquine or hydroxychloroquine. For now, except for supportive measures, infection with SARS-CoV-2 is "essentially untreatable."

• In silico drug discovery suggest several new candidates targeting ACE-correlated genes

Researchers identified a network of 193 genes, 222 interactions and 36 potential drugs that could have a crucial role for

COVID-19 treatment. Among possible interesting drugs are Nimesulide, Fluticasone Propionate, Thiabendazole, Photofrin, Didanosine and Flutamid.

Virtual screening and repurposing of FDA approved drugs against COVID-19 main protease

Molecular modeling, virtual screening, docking, sequence comparison statistics and phylogenetics of the COVID-19 main protease were investigated. The top 20 candidates comprised a broad-spectrum antiviral (ribavirin), anti-hepatitis B virus (telbivudine), two vitamins (vitamin B12 and nicotinamide) and other miscellaneous systemically acting drugs.

Traditional Indian medicinal plants are proposed as novel therapeutic approaches

The authors discussed virus structure, symptoms of COVID-19, SARS, MERS and common flu, the mechanism behind the infection and its immune response. Further, the current treatment options, drugs available, ongoing trials and recent diagnostics for COVID-19 have been discussed. They suggest traditional Indian medicinal plants as possible novel therapeutic approaches, exclusively targeting SARS-CoV-2 and its pathways.

No new COVID-19 Trials registered over weekend at clinicaltrials.gov
 At time of writing, a total of 436 were active, 23 completed, and 3 posted results.

Other Science

• Understanding pathways to death in patients with COVID-19

Lancet Respir Med.: Flowchart of path to recovery or death. Dying process characteristics: predominant terminal organ failure, proportionality of care in the dying process, and involvement of COVID-19 in the dying process.

• Risk factors for death in patients with COVID-19 associated pneumonia

There was an increased risk of death in patients who were: 65+, had preexisting cardiovascular or cerebrovascular disease, CD3(+) CD8(+) T cells </=75 cell. muL(-1), and cardiac troponin I>/=0.05 ng. mL.

ACE2 polymorphism might explain difference in COVID19 susceptibility

The SARS-CoV-2 virus uses the ACE2 enzyme as entry point into human host cells. Less ACE2 means reduced susceptibility to SARS-CoV-2 infection. Eastern Europeans and Scandinavians, have a form of ACE1 ("D allele") that is associated with reduced expression of ACE2. ACE-1 D-allele frequency may explain ~38% of the variability in prevalence of COVID10 (data for 25 countries). Thus, human host ACE1/ACE2 polymorphism may relate to epidemiological findings.

Serious illness resulting in hospitalization can occur in children

Whereas most COVID-19 cases in children are not severe, serious illness still occurs in this age group. Social distancing and everyday preventive behaviors remain important for all age groups.

• SARS-CoV-2 replicates in lung tissues more efficiently than SARS-CoV

In comparing SARS-CoV-2 and SARS-CoV replication, cell tropism, and immune activation profile, a study found the current coronavirus infected and replicated in lung tissues more efficiently. Both were similar in their targets of type 1 and 2 pneumocytes and alveolar macrophages. However, the SARS-CoV infection was better at induction of interferons and at upregulating pro-inflammatory cytokines and chemokines.

• Viral replication, ACE2, and lung damage

A working theory on the cause of lung damage is that while ACE2 is the mechanism for viral entry, it may also be protective against extensive lung damage as it helps to repair the cells that are damaged in the lung. Those with fewer of these kinds of cells may be at higher risk of severe lung injury.

Phylogenetic network analysis of SARS-CoV-2 genomes traces infection origins

PNAS: Viral sequencing allows tracing of cases. Example: Mexican case infected via Wuhan to Germany to Italy transmission.

COVID-19 Open Research Dataset from the Allen Institute for AI

Relevant publications updated weekly COVID-19 Open Research Dataset (CORD-19) is a free resource from the Allen Institute for AI, being updated weekly, currently over 51,000 scholarly articles including over 40,000 with full text, related to COVID-

19, from PubMed, WHO, bioRxiv and medRxiv. The CORD-19 Explorer (https://cord-19.apps.allenai.org/) is a full-text search engine for the db.

• Additional evidence for association between blood groups and COVID-19

A new study using observational data on 1559 individuals tested for SARS-CoV-2 (682 COV+) with known blood type in the New York Presbyterian (NYP) hospital system found additional evidence for association between blood groups and COVID-19. The authors found that the odds of COVID-19 positive vs negative test results were increased in blood groups A and decreased in blood groups O, consistent with previous results from Wuhan and Shenzhen.

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