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2020-04-29 DAILY UNM GLOBAL HEALTH COVID-19 BRIEFING

Christophe G. Lambert

Shawn Stoicu

Ingrid Hendrix

Lori Sloane

Susan Atlas

See next page for additional authors

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Authors

Christophe G. Lambert, Shawn Stoicu, Ingrid Hendrix, Lori Sloane, Susan Atlas, Anastasiya Nestsiarovich, Praveen Kumar, Nicolas Lauve, Alexandra Yingling, Melissa Cosse, Lauren Tagliaferro Epler, Allison Price, Fiona Nguyen, Ariel Hurwitz, Jenny Situ, Ryen Ormesher, Timothy Campbell, Perez Olewe, Clinton Onyango, Kristine Tollestrup, Cristian Bologa, Jens Langsjoen, Gregory Mertz, and Douglas J. Perkins

DAILY UNM GLOBAL HEALTH COVID-19 BRIEFING

April 29, 2020

Executive Summary

NM cases. NM coronavirus origins. Governor update tomorrow. Temporary drivers licenses. Negative tracing app sentiment. CA reopening plans. US travel screening. Influenza reductions w/COVID control. German flu vaccine prep. 1.5B jobs at risk. National health expenditures. US economy shrinks. Aerosolized virus in hospitals. Cellphone disease spread prediction. Social distancing study. Isolation policy effectiveness. Contact tracing to end AIDS/HIV. Homeless shelter prevalence. Predicting herd immunity. Cooler temperatures reduce transmission. *NEJM* rationing rationalization. ECMO regional planning. Canadian ECMO prioritization. Healthcare worker mental health. Infectious Diseases Society guidelines. US hospitalist guide. Managing pregnancies. Coagulopathy management. Hysteroscopy consensus. Renal transplant immunosuppression. Two RT-PCR alternatives. **Remdesivir RCT success**. Novaferon promising study. Probiotics evidence summary. Tocilizumab rationale. 53 new clinical trials. Continue ACE use. Coagulopathy risk screening. Liver tests predict progression. Stem-cell organoid model. Phylogenetic network analysis. Severity: innate vs. adaptive immunity. ECMO update.

All of our past briefings are maintained in a UNM library repository [here](#).

Our continuously curated practice guidelines in the context of COVID-19 can be found [here](#).

Our continuously curated therapeutic evidence is maintained [here](#).

You may submit content for future briefings [here](#).

NM Highlights

- [New Mexico reports 2 more COVID-19 deaths and 239 new cases](#)

The total positive cases and total deaths in the state are 3,213 and 112, respectively. As of today, the state has performed 65,085 tests, there are 163 individuals currently hospitalized for COVID-19, and 734 COVID-19 cases have recovered. New NMDOH portal featuring epidemiologic breakdown of cases.

- [UNM scientists trace origin of coronavirus in New Mexico to Europe and Australia](#)

Many researchers are studying different strains of virus to trace its origin to a specific country or area. This knowledge can help to identify how long the virus may have circulated undetected in NM. It can also help to guide future public health policy decisions. The virus that caused one of the first COVID-19 cases in NM was closely related to samples found in the Netherlands and Switzerland.

- [NM Governor to provide COVID-19 update Thursday 3 p.m.](#)

Gov. Michelle Lujan Grisham said an update on New Mexico's COVID19 efforts, and the details of the extended public health order will be livestreamed on her Facebook page tomorrow, Thursday (3/30), at 3 PM.

- [New Mexico MVD will email a 90-day temporary drivers licenses](#)

In response to the pandemic, the MVD announced on Tuesday that drivers with expired licenses since 3/11/20 can receive a temporary 90-day license via email. This does not apply to drivers with interlock or DWI temporary licenses, limited licenses due to suspensions, or commercial licenses. Drivers who have not provided an email address to the MVD can get their temporary license through MVD's website.

US Highlights

- [Americans responds negatively to use of COVID tracing app](#)
82% of US population has smartphones. Only half would consider downloading a COVID tracing app considered crucial for re-opening US. Widespread mistrust of developers like Google and Apple. 52% of responders do not approve of Trump's handling of COVID. Poll responders approve of social distancing.
- [California Governor outlines plans to reopen the state](#)
Governor Newsom said that the first stage is still to maintain the home state and wait for the rising curve to be stable. The second stage will begin to open low-risk workplaces, such as the retail industry that cannot remotely work, and hopes that the school will reopen at the end of July and early August. In the next stage of opening, gyms, salons and other businesses that require close contact with customers will be opened in a few months instead of weeks.
- [US will screen international air travelers coming from heavily infected areas](#)
International passengers arriving at US airports from a heavily infected places may soon be required to undergo temperature and virus checks to help stop the spread of the coronavirus. Trump said it has not been determined yet whether the federal government or the airlines would conduct the testing. "Maybe it's a combination of both," he said.

International Highlights

- [Decreased influenza incidence under control measures in Singapore](#)
Surveillance data on influenza like illnesses (ILI) in Singapore showed influenza activity declined substantially after public health measures (including public education and physical distancing) were taken to reduce spread. Compared to previous years, estimated daily cases of ILI decreased by 76% in February-March. Surveillance data included number of visits to clinics for ILI per day, ILI samples tested per week, and percentage influenza positivity.
- [Collateral benefit of COVID-19 control measures on influenza activity, Taiwan](#)
Taiwan has strictly followed infection control measures to prevent spread of coronavirus disease. Meanwhile, nationwide surveillance data revealed drastic decreases in influenza diagnoses in outpatient departments, positivity rates of clinical specimens, and confirmed severe cases during the first 12 weeks of 2020 compared with the same period of 2019.
- [Germany buys more flu jabs to spare health system double illness wave](#)
Germany announced measures to help ready the healthcare system, including making 30% more flu jabs available for the autumn flu season. All employees providing elderly care will receive a 1,500-euro bonus, which will be covered by the federal government, states, social insurance, and employers.

Economics, Workforce, Supply Chain, PPE Highlights

- [More than 1.5 billion people risk losing livelihoods](#)
The International Labor Organization warns that two billion workers have seen wages fall by 60%. Those with informal work arrangements, in retail, manufacturing and food service industry are most likely to be affected.
- [The potential effects of coronavirus on national health expenditures](#)
The cost of treating patients with COVID-19 is the smallest component of the economic burden of the pandemic. The much greater costs are the human consequence of disease for individuals and their families and the enormous cost of the precautions taken by individuals and societies to avoid this disease. Most of the economic costs of the pandemic are outside the health care system.
- [US economy sinks 4.8% in the first quarter, expected to sink 30% in second quarter](#)
This was the first contraction since 2014, and further contraction is expected since many restrictions were not in place until March. Consumer spending, which makes up 2/3 of the US economy, dropped 7.6% as spending on food services, accommodation, and clothing plummeted. Healthcare spending was also reduced, as doctors postponed routine care and elective treatments. The US has responded with more than \$3 trillion in new spending. The Federal Reserve has cut interest

rates to a range of 0% to 0.25% and is using emergency powers to expand bond purchases and lending.

Epidemiology Highlights

- [Levels of aerosolized SARS-CoV-2 in two Wuhan hospitals](#)

Nature: Measurement of viral RNA in aerosols of two Wuhan Hospitals in February and March showed high aerosolized viral levels in two public areas prone to crowding and patient toilet areas, low levels in isolation wards and ventilated patient rooms, and undetectable levels in the majority of public areas and sanitized medical staff areas. While the infectivity of the aerosolized virus was not established, this study demonstrates the potential of aerosol transmission, and shows that measures like room ventilation, open space, and proper sanitization/disinfection can limit the concentration of the virus in aerosols.

- [Epidemiological model from mobile phone data accurately predicts disease spread out of Hubei](#)

The authors created a model using about 12 million users' mobile phone location data points from Jan 1 through Jan 24 in Wuhan to estimate disease spread. Population flow out of Wuhan and Hubei province predicts infections in neighboring Chinese cities through Feb 19. Quarantine measures reduced population outflow of Hubei by 94% on Jan 24.

- [Model shows social distancing is sufficient to control COVID-19](#)

An analysis of ~ 2500 contacts evenly split between Wuhan and Shanghai before and after the implementation of social distancing measures. The study provides evidence that the interventions put in place in Wuhan and Shanghai, and the resulting changes in human behavior, drastically decreased daily contacts, essentially reducing them to household interactions. This leads to a dramatic reduction of SARS-CoV-2 transmission.

- [Policies and isolation measures have been effective outside Hubei Province](#)

The analysis of 7,015 confirmed cases found evidence that various policies and isolation measures have been effective since the outbreak of COVID-19. Imported cases started to decrease after traffic restrictions were imposed, and the incubation period gradually increased.

- [Contact tracing for COVID-19 is an opportunity to reduce health disparities and end HIV/AIDS epidemic](#)

Testing and contact tracing as safe and effective COVID-19 public health strategy may provide a unique opportunity to also conduct widespread HIV testing, among other health promotion activities to reduce health disparities and end the HIV/AIDS epidemic in the US.

- [High prevalence of COVID-19 in homeless shelter in Boston](#)

Homelessness creates the potential for rapid transmission of SARS-CoV-2 in vulnerable populations. Boston Health Care for the Homeless Program study revealed that of 408 participants, 36.0% were positive for SARS-CoV-2. These findings illustrate the rapidity with which COVID-19 can be widely transmitted in a homeless shelter setting.

- [Modeling to predict potential pandemic size and herd immunity](#)

This model compares trends in historical mass outbreaks with SARS-CoV-2. The durability of immunity is not yet known and is predicted that it will circulate in humans for many years to come. The challenge is to identify measures that could provide the best protection with less social cost. This study predicts that R0 will exceed the threshold for herd immunity.

- [Most infections From December to March occurred in cooler, cloudier locations](#)

Authors analyzed data collected from the Program for Monitoring Emerging Disease collected from December through March 10, 2020 in cities with at least 500 cases. 90% of community infections occurred in a temperature range of 5-15 C (41-59 F). In Beginning at an UV index of 2.5, infections decreased and are very uncommon at UV index of 5. Precipitation and relative humidity had no effect on the observed number of infections.

- [Negative association between higher temperature and COVID-19 risk in China](#)

The overall epidemic intensity of COVID-19 reduced slightly following days with higher temperatures with a relative risk (RR) was 0.96 (95% CI: 0.93, 0.99). A random-effect meta-analysis including 28 provinces in mainland China confirmed the statistically significant association between temperature and RR during the study period (Coefficient = -0.0100, 95% CI: -0.0125, -0.0074).

Healthcare Policy Recommendations

- [NEJM allocating scarce resources](#)
Initial article outlines four values for allocation of resources: maximizing the benefits produced by scarce resources, treating people equally, promoting and rewarding instrumental value, and giving priority to the worst off. Responses (letter to editor) point out that applying these values requires judgment that is subject to discriminatory social bias, as well as other practical concerns for putting ethical frameworks into practice. Various commentaries: <https://doi.org/DOI:10.1056/NEJMc2009666>
- [Regional planning for extracorporeal membrane oxygenation allocation](#)
The authors developed a framework for integrating ECMO into disaster preparedness planning for COVID-19. They provide guidance on ECMO allocation based on 3 tiers of predicted survival.
- [Extracorporeal life support during COVID-19: practical considerations for Canada](#)
Patients with COVID-19 with refractory hypoxemia despite lung protective ventilation should be considered for extracorporeal life support (ECLS). In Alberta, the authors have developed a red-yellow-green dashboard to indicate capacity and readiness criteria for ECLS utilization, with green indicating use would not impact other services (critical care or cardiac surgery), yellow indicating a state of rationing, and red indicating max ECLS capacity.
- [Mental health problems faced by healthcare workers due to the COVID-19 pandemic-A review](#)
A systematic review found several socio-demographic variables like gender, profession, age, place of work, department of work and certain psychological variables like poor social support and self-efficacy to be associated with increased reporting of stress, anxiety, depressive symptoms, and insomnia in HCW. Authors highlight the need for regular screening and examination of HCW involved in the treatment and diagnosis of patients with COVID-19.

Practice Guidelines

- [Treatment and management for COVID-19 patients: Infectious Diseases Society of America guidelines](#)
The guideline provides 7 COVID-19 treatment recommendations: 1) hydroxychloroquine (HCQ)/chloroquine in context of a clinical trial, 2) HCQ + Azithromycin ONLY in context of a clinical trial, 3) lopinavir/ritonavir ONLY in context of a clinical trial, 4) suggestion against corticosteroids for COVID pneumonia, 5) suggestion against corticosteroids for COVID ARDS, 6) tocilizumab ONLY in context of clinical trial, and 7) convalescent plasma in context of clinical trial.
- [US guide for hospitalists for inpatient care](#)
A review is presented by Mayo Clinic researchers summarizing current information on how hospitalists should approach caring for patients with suspected or confirmed disease. Supportive care is the mainstay of therapy. Interventions to help a health system prepare include establishing a committee for logistic planning and information dissemination, creating a service dedicated to caring for patients with COVID-19, and building contingency plans for anticipated staffing needs.
- [International recommendations for diagnosing and managing pregnant women during COVID-19](#)
Pregnant women should be considered as a high-risk population for COVID-19 infection, and if suspected or proven to be infected with the virus, they require special care. Recommendations are provided on pregnancy and labor management, diagnosing COVID-19, and hospitalization. Pregnancy complications, fetal risks, maternal outcomes, and organization of health care facility are discussed.
- [International guidance on recognition and management of coagulopathy in COVID-19](#)
The International Society of Thrombosis and Haemostasis (ISTH) provides guidance for risk stratification at admission for coagulopathy risk and chemoprophylaxis in COVID-19. Their algorithm utilizes d-dimer, prothrombin time, platelet count, and fibrinogen lab tests to help guide clinical decision making in this regard.
- [COVID-19 and hysteroscopy: Global Congress of Hysteroscopy consensus](#)
Procedures in which delay could worsen the patient's outcome must be performed. Adequate triage of patients with suspected cancer is critical. When possible, use conscious sedation or regional anesthesia to avoid the risk of viral dissemination at the time of intubation/extubation.

- [COVID-19 in renal transplantation: a review supports corticosteroid-sparing immunosuppression](#)

This review compares inpatient immunosuppressant management strategies, and limitations of corticosteroid use. Renal transplant recipients with moderate oxygen requirements can be successfully managed with steroid-sparing immunosuppression including modest reduction of calcineurin inhibitor trough concentrations and antiproliferative dosing.

Testing

- [More accurate CRISPR–Cas12-based lateral flow assay for detection of SARS-CoV-2](#)

Authors report development of rapid (<40min) and accurate CRISPR–Cas12-based lateral flow assay for detection of SARS-CoV-2 from respiratory swab RNA extracts. CRISPR-based DETECTR assay reported to provide visual and faster alternative to CDC's SARS-CoV-2 real-time RT–PCR assay. 95% positive predictive agreement and 100% negative predictive agreement.

- [COVID-19 Ag Respi-Strip Compares Favorably to qRT-PCR](#)

The COVID-19 Ag Respi-Strip represents a promising rapid SARS-CoV-2 antigen assay for the first-line diagnosis in 15 minutes. Its sensitivity and specificity are 57% and 99% respectively. Its role is complementary to current molecular techniques.

Drugs, Vaccines, Therapies, Clinical Trials

- [NIH, Gilead, Fauci announce successful remdesivir randomized placebo-controlled trial n=1063](#)

NIH Data safety and monitoring board (DSMB) recommended study termination based on clear clinical benefit with significant shortening of median recovery time from 15 days to 11 days ($p < 0.001$). There was a trend toward reduced mortality in the treatment group (8% Tx vs 11.6% placebo, $p = 0.059$). The recommendation was based on data available to the DSMB last week, so additional endpoint data is likely to be available when the manuscript is drafted. [Gilead](#) and [NIH](#) announce results early, with NIAID Director Dr. Anthony Fauci discussing the results in a [White House interview](#). DSMB saw clear clinical benefit and notified study team so people on placebo could be offered drug. Dr. Fauci remarked that this reminded him of the initial results with AZT treatment of AIDS, which were followed by improved efficacy as additional drugs came on line. In light of demonstrated clinical efficacy of remdesivir, Dr. Fauci noted that future randomized controlled trials (RCTs) will have to include remdesivir rather than placebo once remdesivir is available. Gilead exploratory analysis supports earlier treatment: patients in the study who received remdesivir within 10 days of symptom onset had improved outcomes compared with those treated after 10 days. Most common adverse events occurring in >10% of patients in either group were nausea (5-day: 10.0%, $n = 20/200$ vs. 10-day: 8.6%, $n = 17/197$) and acute respiratory failure (5-day: 6.0%, $n = 12/200$ vs. 10-day: 10.7%, $n = 21/197$). Grade 3 or higher liver enzyme (ALT) elevations occurred in 7.3% ($n = 28/385$) of patients, with 3.0% ($n = 12/397$) of patients discontinuing remdesivir treatment due to elevated liver tests. This report comes after a smaller ($n = 237$) Chinese RCT published in *Lancet* (that did not meet its target accrual due to reduction in local cases) showed similar trends in efficacy but failed to show significance.

- [Novaferon in randomized parallel group study outperforms lopinavir/ritonavir for viral clearance](#)

MedRxiv preprint: Novaferon, a novel protein drug approved for the treatment of chronic hepatitis B in China, was shown to inhibit viral replication in infected cells and enable healthy cells to resist viral entry. In a small randomized, open-label, parallel group study ($n = 89$), both Novaferon alone and Novaferon with Lopinavir/Ritonavir groups had significantly higher clearance rates on day 6 than the Lopinavir/Ritonavir group (50.0% vs. 24.1%, $p = 0.0400$, and 60.0% vs. 24.1%, $p = 0.0053$).

- [Evidence summary for probiotics in treatment of COVID-19](#)

A brief correspondence letter in the *Lancet* summarizes existing evidence for use of probiotics in COVID-19. Probiotics are routinely used for COVID care in China, and RCTs have shown reduction in ventilator associated pneumonia from probiotics versus placebo. Not all probiotics are the same.

- [Rationale for use of Tocilizumab in the treatment of coronavirus pneumonia](#)

Clinical Drug Investigation: The authors discuss the role of cytokine storm in Covid-19; the mechanism of Tocilizumab, an IL-6 receptor antagonist, in treatment; and key points of pharmaceutical case based on clinical application. The role of Tocilizumab in treating the virus currently remains unclear.

- [53 New COVID-19 Trials registered today at clinicaltrials.gov](#)

Treatment trials: Seroprevalence and Mental Health Burden, Repurposing of Chlorpromazine, Enoxaparin for Thromboprophylaxis, Neuroradiological, Rapid Detection of COVID-19 by Portable and Connected Biosensor, Vagus Nerve Stimulation, Fungal Infections, Molded Flocked Nasopharyngeal Swabs, Hepatocellular Carcinoma, Caldifediol, intermediate or Prophylactic-Dose Anticoagulation for Venous or Arterial Thromboembolism, Immune Repertoire Sequencing, Enhanced Platelet Inhibition, Influenza Vaccination, ADEI and ARB, Thrombo Embolic Events, Bacteriotherapy, Effects of Attention Training on Emotion Regulation and Stress Related Complaints, Colchicine. At time of writing, a total of [1015](#) were active, [48](#) completed, and [3](#) posted results.

Other Science

- [Clinical impact of renin-angiotensin system inhibitors on mortality of patients with hypertension remains unknown, continue current hypertensive medication regimen](#)

Clinical Infectious Diseases (Letter to editor): Researchers studied a cohort of 311 patients with hypertension and confirmed COVID diagnoses across 10 hospitals in Italy. 131 of the 311 patients died while hospitalized. They found that the sequential organ failure assessment (SOFA) score and age were greater predictors of in-hospital mortality, whereas the chronic use of renin-angiotensin system inhibitors was not associated with this outcome. Patients are recommended to continue their current hypertensive medications pending results of randomized control trials addressing impact of RASIs.

- [Coagulation test screening, including the measurement of D-dimer and fibrinogen levels, is suggested](#)

The initial coagulopathy of COVID-19 presents with prominent elevation of D-dimer and fibrin/fibrinogen degradation products, while abnormalities in prothrombin time, partial thromboplastin time, and platelet counts are relatively uncommon in initial presentations. Coagulation test screening, including the measurement of D-dimer and fibrinogen levels, is suggested. Current data do not suggest the use of full intensity anticoagulation doses unless otherwise clinically indicated. Even though there is an associated coagulopathy with COVID-19, bleeding manifestations, even in those with DIC, have not been reported.

- [Patients with abnormal liver tests are at higher risks of progressing to severe disease](#)

In this meta-analysis of 37 studies (n=6235), patterns of COVID-19 disease severity relative to hepatocellular injury, cholestasis, and synthetic dysfunction are described. The pooled mean of alanine aminotransferase was 36.4 IU/L in severe cases and 27.8 IU/L in non-severe cases (95% CI: -9.4- -5.1, p<0.0001). Pooled average of aspartate aminotransferase was 46.8 IU/L in severe cases and 30.4 IU/L in non-severe cases (95% CI: -15.1- -10.4, p<0.0001). The severe cases tended to have higher γ -Glutamyl transferase and lower albumin. Monitoring of liver chemistries provides early warning against disease progression.

- [Potential ex vivo model of viral lifecycle using human induced pluripotent stem cell-3D organoids](#)

Organoids derived from human induced pluripotent stem cells (iPSCs) may serve as suitable infection models for ex vivo mimicking of the viral life cycle and drug screening. The authors suggest the use of a functional human iPSC-organoid that could act as a reliable and feasible ex vivo infection model for investigation of the virus. This approach will provide insight into the underlying molecular dynamics of COVID-19 for the of novel treatment and prevention strategies.

- [Phylogenetic network analysis method of choice for SARS-CoV-2 genome evolution](#)

Application of phylogenetic techniques and mutational analysis to 160 SARS-CoV-2 genomes from the GISAID database (<https://www.gisaid.org/>) to trace virus evolution from common ancestor(s), and track global virus spread. Because parallel evolutionary events are happening in humans, character-based phylogenetic networks are the method of choice for reconstructing viral evolutionary paths and their ancestral genome in the human host.

- [Severe cases showed increased markers for innate immune response and decreased markers for adaptive immune response](#)

A systematic review and meta-analysis of 45 studies investigated severe and critical cases and found increased markers for innate immune responses, tissue damage, and major organ failure, and decreased markers for adaptive immune response. The authors report: higher neutrophil count (MMD: 1.23 [95% CI: 0.58 to 1.88] $\times 10^9$ cells/L), lower lymphocyte count

(MMD: -0.39 [95% CI: -0.47, -0.31] $\times 10^9$ cells/L, and lower CD4 counts (MMD: -204.9 [95% CI: -302.6, -107.1] cells/uL). Other results of severe/critical COVID-19 disease include C-reactive protein (MMD: 36.97 [95% CI: 27.58, 46.35] mg/L), interleukin-6 (MMD: 17.37 [95% CI: 4.74, 30.00] pg/ml), and Troponin I (MMD: 0.01 [0.00, 0.02] ng/ml), and D-dimer (MMD: 0.65 [0.45, 0.85] mg/ml).

- [Extracorporeal membrane oxygenation for critically ill patients: update](#)

Data on ECMO in COVID-19 patients (n=333) reported by the European Extracorporeal Life Support Organization (EuroELSO) were analyzed for the incidence of death during ECMO. Death rate was 17.1% (95% CI: 13.1% to 21.1%). Exploratory inferential analysis showed no statistically significant association between death and gender ($p=0.788$), but age showed a significant correlation, especially in patients >60 years (odds ratio: 4.80 [95% confidence interval 1.64 to 14.04], $p=0.004$)

Contributing team members: Christophe G. Lambert, Shawn Stoicu, Ingrid Hendrix, Lori Sloane, Susan Atlas, Anastasiya Nestsiarovich, Praveen Kumar, Nicolas Lauve, Alexandra Yingling, Melissa Cossé, Lauren Tagliaferro Epler, Allison Price, Fiona Nguyen, Ariel Hurwitz, Jenny Situ, Ryen Ormesher, Timothy Campbell, Perez Olewe, Clinton Onyango, Kristine Tollestrup, Cristian Bologna, Jens Langsjoen, Gregory Mertz, Douglas J. Perkins.