4-19-2020

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

Christophe G. Lambert
University of New Mexico Health Sciences Center

Shawn Stoicu

Ingrid Hendrix
University of New Mexico

Anastasiya Nestsiarovich

Praveen Kumar

See next page for additional authors

Authors

Christophe G. Lambert, Shawn Stoicu, Ingrid Hendrix, Anastasiya Nestsiarovich, Praveen Kumar, Nicolas Lauve, Rachel D. King, Samuel Anyona, Evans Raballah, Cristian Bologa, Alexendra Yingling, Orrin Myers, Andrew S. Rowland, and Douglas J. Perkins

DAILY UNM GLOBAL HEALTH COVID-19 BRIEFING

April 18-19

Executive Summary

NM highlights. Census under-counting. Zip code cases. NM Volunteers needed. Jury trials suspended. Tracking NM cases. Tribal susceptibility & response. Shortages: Legal guidance. Life insurance pause. US case geography. Korean 2.1% reinfection. International policy review. Research disruption. Neuropsychiatric sequelae looming. Case undercounting. Antibody test utility. Air travel infection. FDA serologic test guidance. Household transmission. Human behavior & public health. Military leadership principles. Systematic review quality. Clozapine consensus. Guidelines for: nasopharyngeal swabs, tracheostomy, intubation, extubation, managing laryngectomy patients, stroke thrombectomy, cardiac surgery, neuroanesthesia, coagulopathy management, ECMO, radiology safety, nuclear medicine, gastroenterology, and grief in palliative care. Hydroxychloroquine and antivirals fail to show benefit. Review on drug repurposing. Viral load symptom onset. Lymphocytes & case severity. Reactive lymphocytes. Saliva testing. Blood test Dx alternative. RT-PCR + clinical suspicion. Sperm tests negative. Thrombocytopenia mechanisms. Smell dysfunction. No rhesus macaque reinfection. Respiratory center damage.

NM Highlights

- 2 new deaths and 47 additional COVID-19 cases reported in New Mexico according to partial report

  The total positive cases and total deaths in the state are 1,845 and 55, respectively. As of today, the state has performed 37,042 tests, there are 103 individuals hospitalized for COVID-19, and 487 COVID-19 cases have recovered. New NMDOH portal featuring epidemiologic breakdown of cases.

- US census rural NM under-counting amid pandemic jeopardizes decade of future state funding

  Pandemic curtails census workers reaching rural New Mexicans. A full count is required to receive NM's share of hundreds of billions of dollars in federal funding for its communities for the next decade, impacting healthcare, education, infrastructure and transportation services for years to come.

- How many infected in your neighborhood? NMDOH public dashboard gives cases by zip code

  The state added the new feature of its data dashboard Friday. The state also breaks down cases by county by testing and lists cases according to gender, age and ethnicity.

- Volunteers needed across the state -- people can often help from home

  Albuquerque launched a volunteer portal online at the end of March. Among the places seeking help are Meals on Wheels, Mask Drive New Mexico 2020 is recruiting volunteers with sewing skills to make masks. Volunteers sought for screenings at the West Side Homeless shelter and Roadrunner Food Bank. They are having all volunteers honor social distancing.

- NM Supreme Court extends suspension of jury trials until May 29 because of COVID-19 outbreak

  Conflict between individual civil liberties and public health. Chief Justice Judith K. Nakamura said in a written statement citing need to protect public health and control the spread of COVID-19. Concerns from NM Criminal Defense Lawyers Association that continued delay will trample the rights of defendants who are awaiting trial in custody. Concerns somewhat offset by proviso that suspension of trials is "subject to the individual discretion of the judges presiding in such cases to go forward … to avoid serious harm to the interests of the litigants or for other exceptional circumstances."

- UNM Scientists use genome sequencing to track origin of NM cases

  Drs. Darrel Dinwiddie and Daryl Domman have sequenced 48 viral genomes from New Mexico and have 1,400 more ready for testing. Preliminary analysis suggests there were multiple introductions of the virus into the state, which is consistent with

early reports of cases among people who had traveled abroad or domestically.

- Susceptibility of southwestern American Indian tribes to COVID-19

  UNM Internal Medicine physicians, Monika Kakol, Dona Upson, and Akshay Sood highlight factors which may be contributing to the increased impact on tribes such as genetic susceptibility, immunologic naivety, social determinants of health and comorbidities.

- Video: government leaders discuss state response to COVID-19 in tribal communities

  Sunday evening, Sec. Trujillo, President Nez, Congresswoman Haaland, and others discuss the states response to COVID-19 in Tribal Communities, including the Navajo Nation.

US Highlights

- Lawyers say triage guidance is urgently needed in event of shortages

  US Medical Protection Society has called for the introduction of emergency laws to protect doctors and their clinical decisions, as New York state has done -- see March 26 NY Governor executive order granting certain legal protections to healthcare workers: Internal URL: https://www.mlmic.com/blog/physicians/new-york-physician-immunity-during-pandemic

- Some life insurers pause new policies for older Americans

  Some insurers are temporarily suspending applications for individuals in their 60s who previously may have been eligible for coverage despite common health problems and those aged 70 or older.

- Geographic distribution in the US: cases, deaths, and incidences

  As of April 7, cumulative incidence across the U.S. varies from 20.6 to 915.3 cases per 100,000 and the increase of 7-day incidence ranges from 8.3 to 418.0 cases per 100,000. The report describes the geographic distribution of laboratory-confirmed cases and related deaths reported in U.S. jurisdictions during February 12-April 7, 2020.

International Highlights

- Korean CDC reports 2.1% retest positive after discharge, 44% symptomatic -- all mild

  As of April 17, 163 (2.1%) of the 7,829 cases that have been discharged from isolation have tested positive again after an average of 13.5 days (range: 1-35 days). 61 (43.9%) of retested-positive cases were symptomatic, all of which showed mild symptoms. No secondary infection has been reported, and viral cultures have failed to grow thus far (n=6). In general, retested-positive cases are handled the same as first-time confirmed cases.

Economics, Workforce, Supply Chain, PPE Highlights

- The role of national and international institutions and policy makers in COVID-19

  A review of the immediate response of different national and international institutions and authorities to the pandemic.

- Disruption in grand-funded work due to coronavirus outbreak

  The coronavirus outbreak has forced the closure of labs and universities. Researchers are confined to their homes and are unable to carry on with grant-funded work. Because of the disruption researchers face challenges in completing projects by their deadlines and might struggle to pay lab members when grants run out.

Epidemiology Highlights

- Potential for large-scale neuropsychiatric sequelae of COVID-19

  Past pandemics have had a large fallout in terms of host immunologic response to infection, on the human central nervous system (CNS) and related neuropsychiatric outcomes. Early reports from China suggested nearly half of severe cases had neurologic complications (e.g., stroke), encephalopathies, and muscle injuries. In the past, in utero viral exposures have been linked to increased risk of schizophrenia so that is a potential concern. Survivors of SARS-CoV-1 were clinically diagnosed with PTSD (54.5%), depression (39%), pain disorder (36.4%), panic disorder (32.5%), and obsessive compulsive disorder

(15.6%) at 31 to 50 months post-infection, a dramatic increase for pre-infection prevalence of any psychiatric diagnoses of 3% (Lam, 2009). The need for sustained follow-up of psychiatric symptoms related to SARS-CoV-2 infection, beyond documenting acute stress levels, is therefore paramount and urgent.

- Antibody tests suggest a more than 50-fold increase in coronavirus infections compared to official cases

  An analysis of the blood of some 3,300 people living in Santa Clara county found that one in every 66 people had been infected with SARS-CoV-2. On that basis, the researchers estimate that 48,000-82,000 inhabitants of the county were infected with the virus — numbers that contrast sharply with the official case count of some 1,000 people reported in early April. The findings suggest that because many asymptomatic cases are going undetected, the case fatality rate have been over-estimated. However, some scientists have raised concerns about the accuracy of antibody tests used in these studies because most have not been rigorously assessed to confirm they are reliable.

- Problems with antibody tests continue to limit their usefulness

  Many of the antibody tests being introduced in the U.S. come from China and have not been tested and approved by the FDA. Scientists are finding the tests can often be inaccurate, particularly rapid tests being employed in physician's offices. The problem seems to be that not enough work has been done to standardize and validate the tests. Once the tests are validated, experts anticipate additional challenges getting the raw materials needed and the tests distributed. Many agree that antibody tests will play an important role in decision making about restarting the economy. However, the World Health Organization does not recommend use of the tests at this time. More scientific work needs to be done to increase test reliability.

- The association between international and domestic air traffic and the coronavirus outbreak

  The number of flight routes as well as total passenger volume are highly relevant risk factors for the spread of current COVID-19, particularly flights from China. Multiple regions within Asia, as well as some in North America and Europe are at serious risk of new exposures to COVID-19 from China and other highly infected countries. Risk for COVID-19 exposure remains relatively low in South America and Africa but that could change.

- US FDA provides an update on serological test validation and education efforts

  There are currently important concerns about serological tests that are now on the market. Because antibody tests may be important in the nation's response efforts, the US FDA is providing further details about their approach to making accurate and reliable serology tests widely available, while also protecting Americans from tests marketed with false or unsubstantiated claims.

- The characteristics of household transmission of COVID-19

  The secondary attack rate of SARS-CoV-2 in household is 16.3%. Ages of household contacts and spouse relationship with index case are risk factors for transmission of SARS-CoV-2 within household. Quarantine of index patients at home since onset of symptom is useful to prevent the transmission of SARS-Co-2 within household.

Healthcare Policy Recommendations

- Large review on aligning human behavior with public health interests

  Evidence assembled from a selection of research topics relevant to pandemics, including navigating individual vs. collective interests, threats, social and cultural influences on behavior, science communication, moral decision-making, leadership, and stress and coping. Each section, notes the nature and quality of prior research, including uncertainty and unsettled issues. Direct download of preprint here: https://psyarxiv.com/y38m9/download Insights include: • A shared sense of identity or purpose can be encouraged by addressing the public in collective terms and by urging "us" to act for the common good. • Identifying sources (e.g., religious or community leaders) that are credible to different audiences to share public health messages can be effective. • Leaders and the media might try to promote cooperative behavior by emphasizing that cooperating is the right thing to do and that other people are already cooperating. • Norms of prosocial behavior are more effective when coupled with the expectation of social approval and modeled by in-group members who are central in social networks. • Leaders and members of the media should highlight bipartisan support for COVID-related measures, when they exist, as such endorsements in other contexts have reduced polarization and led to less biased reasoning. • There is a need

for more targeted public health information within marginalized communities, and for partnerships between public health authorities and trusted organizations that are internal to these communities. • Messages that (1) emphasize benefits to the recipient, (2) focus on protecting others, (3) align with the recipient's moral values, (4) appeal to social consensus or scientific norms, and/or (5) highlight the prospect of social group approval tend to be persuasive. • Given the importance of slowing infections, it may be helpful to make people aware that they benefit from others' access to preventative measures. • Preparing people for misinformation and ensuring they have accurate information and counterarguments against false information before they encounter conspiracy theories, fake news, or other forms of misinformation, can help 'inoculate' them against false information. • Use of the term "social distancing" might imply that one needs to cut off meaningful interactions. A preferable term is "physical distancing," because it allows for the fact that social connection is possible even when people are physically separated.

- Applying principles of military leadership to the Covid-19 crisis

  The key components of mission command are unity of effort, freedom of action, trust, mutual understanding and rapid decision making.

- Poor quality of most of systematic reviews on COVID-19. 49 systematic reviews (SR) are analyzed

  The methodological quality of most SRs on coronavirus outbreaks is unsatisfactory, and those on COVID-19 have higher risks of poor quality, despite the rapid actions taken to conduct SRs. The quality of SRs should be improved in the future. Readers must exercise caution in accepting and using the results of these SRs

- Risk mitigation against COVID-19

  The risk mitigation measures taken by various countries are analyzed. These include: mobility restrictions, physical distancing, hygienic measures, socio-economic restrictions, communication and international support mechanisms. The quantitative effectiveness of each measure is not yet apparent. Initial impacts of global risk mitigation measures taken during the combatting of the COVID-19 pandemic.

Practice Guidelines

- Consensus statement on the use of clozapine during the COVID-19 pandemic

  Recommendations from the international expert advisory subgroup of the Treatment Response and Resistance in Psychosis working group. Due to risk of clozapine-associated severe neutropenia, absolute neutrophil count (ANC) monitoring programs are a prerequisite for clozapine dispensation in most jurisdictions globally. They recommend: 1) Reduction in testing to once per 3 months if patient on drug for 1 year and has had no ANC issues, or if safe testing not practical; 2) Immediate exam, including CBC if COVID-19 symptoms appear; 3) Reduce dosage by as much as 1/2 if COVID-19 symptoms appear, due to risk of toxicity of rising clozapine levels during acute infection, stepping dosage up incrementally after symptoms resolve.

- The video instructions on how to obtain a nasopharyngeal swab specimen

  The 5-minute video shows how to perform the procedure.

- Tracheostomy procedure during the Covid-10 outbreak

  The surgeons' modified guidelines are: 1) all procedures should be done under general anesthesia, with deprivation of spontaneous respiration and application of muscle relaxants, regardless of whether patients had spontaneous breathing or not; 2) after the cervical trachea is exposed and immediately before an incision is made in the trachea, the endotracheal tube is inserted deeper, positioned with the tip close to carina of the trachea; 3) when the opening is complete, brief interruption of the ventilator is essential.

- New methods for safe intubation while managing patients with COVID-19

  Current intubation recommendations focus on high-efficiency particulate air (HEPA) filter usage connected between the bag valve and the patient mask during preoxygenation. After intubation, the HEPA filter is then disconnected from the bag valve mask and reconnected to the endotracheal tube (ETT). The authors suggest using a closed system with the HEPA filter already attached to the ETT via either the HEPA-ETT ('HE') or 'Swivel-HEPA-ETT (SHE)-bougie' methods. The ETT combination with HEPA filter in advance can potentially reduce aerosolization of the viral droplets from the larynx and trachea during

intubation, and the ventilator can then be connected directly to the HEPA filter after intubation. These two methods can also allow for confirmation of ETT placement without auscultation, which may be difficult to perform while wearing PP.

- Extubation of patients with COVID-19

  The authors propose extubation guidelines for COVID-19 patients aimed at minimizing staff exposure to SARS-CoV-2.

- Management of total laryngectomy patients during the COVID-19 pandemic

  The guide is provided, including the flowchart for determining approach to tracheoesophageal prostheses (TEP). The possible complications, as well as recommendations for rigorous PPE are described.

- Stroke thrombectomy recommendations during COVID-19

  The Society of NeuroInterventional Surgery provides the recommendations on the management of stroke thrombectomy with an emphasis on safety measures for healthcare providers.

- Canadian Society of Cardiac Surgeons guidelines on cardiac surgery

  The Canadian Society of Cardiac Surgeons (CSCS) and its Board of Directors have come together to formulate a series of guiding statements to help to their colleagues on the subjects of leadership, patient triage and risk reduction.

- Society for Neuroscience in Anesthesiology & Critical Care (SNACC) guidelines for neuroanesthesia

  This consensus statement provides information on the neurological manifestations of COVID-19, advice for neuroanesthesia clinical practice during emergent neurosurgery, interventional radiology (excluding endovascular treatment of acute ischemic stroke), transnasal neurosurgery, awake craniotomy and electroconvulsive therapy.

- Society of Thrombosis and Haemostasis guidelines on coagulopathy management in COVID-19

  The International Society of Thrombosis and Haemostasis provides the guidelines for risk stratification at admission for a COVID-19 patient and management of coagulopathy which may develop in some of these patients, based on easily available laboratory parameters.

- Extracorporeal membrane oxygenation therapy in the COVID-19 pandemic

  A review of ECMO as a mechanical support option in COVID-19 patients with critical disease is provided.

- Prevention and control measures in radiology department during COVID-19 pandemic

  The authors summarize the consensus recently presented under the endeavors of radiologists and radiological technologists led by the Chinese Society of Imaging Technology, Chinese Medical Association, aiming to guide the prevention and practical work in the radiology department.

- Singapore radiology department strategies to prevent COVID-19 spread

  The authors' highlights are: 1) Radiology departments should ensure adequate portable imaging capabilities, manpower demands, and PPE stock in this time of outbreak. 2) Strict infection control practices, heightened levels of hygiene, and rigorous cleaning are essential in reducing spread of COVID-19. 3) Physical and temporal staff segregation with deliberate limitation of staff-to-staff interactions.

- "Mass Casualty Incident Planning" to prepare the radiology departments

  The recommendations for developing and implementing a mass casualty incident (MCI) plan for a viral outbreak, such as the current COVID-19. The MCI plan consists of preparation, mobilization of resources, imaging chain, adjusting imaging protocols, and education, such as MCI plan simulation and in-service training. Having an MCI plan in place for a viral outbreak will protect patients and staff and ultimately decrease virus transmission.

- The guidance for nuclear medicine departments

  The guidance is provided based on the systematic review of available literature and the contribution of a panel of international experts of the International Atomic Energy Agency (IAEA). The principles are described for adapting the standard operating procedures until more detailed guidance is prepared by the IAEA.

- Gastroenterology department reorganisation during COVID-19

  This proposal is based on Italian and Chinese experience.

- Grief during the COVID-19 pandemic: considerations for palliative care providers

  Managing grief for providers, patients, and their loved ones is amplified by patient isolation, individual's guilt about the behavior that led to infection, and the fact that patient's loved ones are unable to say good bye and/or participate in funeral rituals. The guidelines for both patients and providers are given, with a table of links to resources on communication, telehealth, advanced care planning, and self-care.

Promising Drugs, Vaccines, Therapies, Clinical Trials

- Meta-analysis of hydroxychloroquine placebo randomized controlled trials fails to show benefit

  MedRxiv preprint: Meta-analysis included 11 RCTs with 2613 adult patients from studies on hepatitis, chikungunya, HIV, dengue, influenza, and COVID-19 (one study). Both the plasma viral load (standard mean difference: 0.29, 95% CI: -1.19-1.76, P = 0.70) and the improvement of clinical symptoms (odds ratio: 2.36, 95% CI: 0.81 - 6.92, P = 0.11) were not statistically significantly different between the intervention and placebo arm. Insufficient data were available to support the antiviral efficacy of CQ and HCQ due to the high heterogeneity caused by the age of patients. Mild side effects are expected for the current antiviral dose regimens of CQ and HCQ (Risk Ratio 1.51, 95% CI: 1.35 -1.70, P<0.05). Treatment outcomes may be enhanced by better-selected patients based on age and well-controlled adverse events.

- No impact of adding antiviral therapies for COVID-19 Pneumonia

  Researchers at the Shanghai Public Health Clinical Center report in the Journal of Medical Virology the peer-reviewed results of a 7-arm randomized clinical trial on 184 COVID-19 patients. The 7 groups included symptomatic treatment, arbidol, lopinavir/ritonavir, arbidol+lopinavir/ritonavir, interferon, Interferon+lopinavir/ritonavir, and interferon+darunavir. No significant differences were found among 7 groups of treatments in terms of the proportion of patients with pneumonia resolution (P=0.151) or the length of hospital stay (P=0.116). Thus, the inclusion of antiviral drugs in therapeutic regimens based on symptomatic treatment had no significant additional impact on the improvement in COVID-19 patients.

- Virus structure, immune response, hyperinflammation: review related to drug repurposing

  In this review, to better gain information about appropriate anti-inflammatory treatments, mostly used in rheumatology for COVID-19, the authors have focused on the structural features of SARS-CoV-2, the host immune response against SARS-CoV-2 and its association with the cytokine storm.

Other Science

- Highest viral load in throat swabs at the time of symptom onset

  Infectiousness predicted to start from 2.3 days before symptom onset and peaked at 0.7 days in Wuhan sample. Secondary cases infected during the index cases' presymptomatic stage (44%), in settings with substantial household clustering.

- Abnormally low lymphocytes levels an effective and reliable indicator of the severity and hospitalization

  Letter to Editor: Lymphocytes express the coronavirus receptor ACE2 and may be a direct target of viruses. Acute lymphocyte decline might be related to lymphocytic dysfunction, and the direct damage of novel coronavirus virus to organs such as thymus and spleen.

- Detection of reactive lymphocytes in COVID-19 patients

  Unlike previous coronavirus responsible for the 2003 SARS outbreak, an examination of peripheral blood films of COVID-19 patients revealed presence of reactive lymphocytes (antigen-stimulated large cytotoxic cells). Reactive lymphocytes were found in 72% of patients with Covid-19 (n = 32).

- SAR-CoV-2 can reliably be detected in saliva by by RT-rPCR analysis

  Saliva from all 25 participants in this Italian study tested positive for SAR-CoV-2. This suggests that saliva tests are promising; it may provide information about the clinical evolution of the disease.

- Routine blood tests as an alternative to RT-PCR for identifying COVID-19

  WBC, platelet, CRP, AST, ALT, GGT, ALP and LDH plasma levels were retrospectively analyzed and related to their

corresponding RT-PCR tests in 207 ER patients suspected for COVID-19. Statistically significant differences b/w positive and negative patient groups were observed for WBC, CRP, AST, ALT and LDH parameters. Empirical thresholds for AST and LDH allowed the identification of 70% of either COVID-19-positive or -negative patients. Blood tests might be used as an alternative to RT-PCR for identifying COVID-19 patients in countries with a shortage of RT-PCR reagents and/or specialized laboratory.

- Importance of combining RT- PCR and clinical features: expert's opinion

  For real-time RT-PCR negative result with clinical features suspicion for COVID-19, especially when only upper respiratory tract samples were tested, multiple sample types in different time points should be tested, including from the lower respiratory tract if possible.

- Coronavirus absent from both the semen and testis specimens at both acute and recovery phases

  The study finds it is highly unlikely that the 2019-nCov can be sexually transmitted by men. No evidence of either sexual or vertical transmission by infected women.

- Hypothesized mechanisms of thrombocytopenia in COVID-19 patients

  High rates of lymphopenia, thrombocytopenia, and leukopenia have been observed, particularly in more severe cases. Three mechanisms are hypothesized: 1) Direct infection of bone marrow cells by the virus and inhibition of platelet synthesis. Following virus infection, cytokine storm destroys bone marrow progenitor cells and leads to the decrease of platelet production. Lung injury indirectly results in reduction of platelet synthesis. 2) Platelet destruction by the immune system. 3)Platelet aggregation in the lungs, resulting in microthrombi and platelet consumption.

- Smell dysfunction is a reliable marker for detecting SARS-Cov-2 infection

  Quantitative smell testing shows 98% accuracy with 95% CI in detecting SARS-CoV-2 infection when using smell dysfunction rather than anosmia as a predictor of COVID-19 infection. The sample size was small but 59 out of 60 COVID-19 patients were identified as having smell dysfunction ranging from mild microsomia to anosmia. This suggests smell dysfunction could be used to identify patients early for treatment and quarantine purposes in areas where current testing methods are scarce.

- Novel fully automated immunoassays

  The aim of this study was to analyze the immunological response to SARS-CoV-2 using novel fully automated chemiluminescence immunoassays (CLIAs).

- No reinfection in SARS-CoV-2 infected rhesus macaques

  Longitudinal tracking of re-exposure after symptoms disappeared in SARS-CoV-2-infected monkeys was performed. The results indicated that the primary SARS-CoV-2 infection could protect from subsequent exposures.

- Coronavirus damage to the respiratory center of the brain

  Letter to the Editor: Respiratory involvement is the most common in patients confirmed with Covid-19, however there are reports of neurological manifestations. Viruses can reach the central nervous system (CNS) through hematogenous or neural propagation and once entered the CNS, viruses can generate alterations in neurons. Presence of the virus in areas of the brain stem, a structure that contains nuclei that regulate the respiratory rhythm.

Contributing team members: Christophe G. Lambert, Shawn Stoicu, Ingrid Hendrix, Anastasiya Nestsiarovich, Praveen Kumar, Nicolas Lauve, Rachel D King, Samuel Anyona, Evans Raballah, Cristian Bologa, Alexandra Yingling, Orrin Myers, Andrew Rowland, Douglas J. Perkins.