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2020-06-15/16 DAILY UNM GLOBAL HEALTH COVID-19 BRIEFING

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DAILY UNM GLOBAL HEALTH COVID-19 BRIEFING

June 15-16, 2020

Executive Summary

NM Highlights: NM case updates. Tribal outreach campaign. Santa Fe firefighters support first responders.

US Highlights: COVID-19 hospitalizations rise in Texas. US retail sales up in May. Projected COVID-19 deaths in US.

International Highlights: COVID-19 prevention and control in Africa. COVID-19 response and challenge in Africa.

Epidemiology Highlights: Herd immunity in Europe. Social distance measures effects. Modeling infections in India. Fecal analysis. Wastewater-based Epidemiology Consortium.

Healthcare Policy Recommendations: Public health approach to lockdown debate. All of Us Program adds new COVID-19 initiatives.

Practice Guidelines: Guidelines are reviewed on urology care. IBD endoscopy. Convalescent plasma use.

Testing: Patient predictors of risk for positive COVID-19 test are reported and an online risk calculator is now available.

Drugs, Vaccines, Therapies, Clinical Trials: Steroid dexamethasone reduces 28-day mortality by 1/3. Research links 'inflamm-aging' and cytokine storm in elderly. Cancer drug may reduce severe COVID-19. 48 new trials registered.

Other Science: Postpone surgery. Proteins predict outcomes. Neurologic manifestations. Thromboembolic risk. Zoonotic transmission. Liver failure. Cardiac complications.

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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

- NM reports 7 more COVID-19 deaths and 88 additional cases on June 16
 - As of today (6/16), the total positive cases and total deaths in the state are 9,933 and 447, respectively. The state has performed 271,553 tests, there are 156 individuals currently hospitalized for COVID-19, and 4,217 COVID-19 cases have recovered. NMDOH portal featuring epidemiologic breakdown of cases.
- New Mexico begins tribal outreach campaign amid coronavirus pandemic
 Santa Fe New Mexican: New Mexico health officials have teamed with Native American cartoonist Ricardo Caté to increase

awareness about the coronavirus pandemic as part of a new campaign. His cartoon, Without Reservation, is published daily in the Santa Fe New Mexican. Officials say the goal is to use culturally relevant messaging on how tribal members can take precautions to protect their communities, families and elders.

• Santa Fe County firefighters union creates nonprofit to support first responders

Santa Fe New Mexican: The Santa Fe County International Association of Firefighters Local 4366 launched the Santa Fe County Firefighters Foundation last week to help raise money for community projects such as firewood drives as well as firefighters and paramedics injured on the job. For more information visit here.

US Highlights

Texas reports record-breaking coronavirus hospitalizations

CNBC News: Texas health authorities said there were 2,287 patients sickened with Covid-19 across its hospitals on Sunday, the sixth new high for coronavirus hospitalizations in the state in less than a week. In the past week, Wednesday was the only day that Texas didn't set a new record for hospitalizations. Texas was among the first states to relax its statewide stay-athome order, allowing it to expire April 30. Infectious disease experts say the steady rise in Covid-19 cases and hospitalizations in Texas and other states will likely add to scrutiny from some U.S. lawmakers that some states opened businesses too early.

• <u>US retail sales bounce up 17.7% as states reopen</u>

NPR: As more states and cities allowed restaurants and shopping centers to reopen, U.S. retail sales — a measure that includes spending on gasoline, cars, food and drink — swung big in May, the U.S. Commerce Department said Tuesday. Spending is still down 6.1% from a year earlier because of the coronavirus pandemic.

Model projects 200,000 COVID-19 deaths in the US by October

CNN: One model cited by the White House now predicts 200,000 deaths from coronavirus by October 1 -- an increase of 30,000 deaths since last week's projection by the Institute for Health Metrics and Evaluation at the University of Washington. Increased mobility and premature relaxation of social distancing led to more infections in Florida, Arizona, and other states.

International Highlights

What works and doesn't in response to COVID-19 prevention and control in Africa

International Journal of Infectious Diseases: The five countries with the highest cumulative number of cases in Africa are South Africa, Egypt, Nigeria, Algeria, and Ghana. The lower number of COVID-19 cases in most African countries may be attributed to inadequate health systems, low-to-absent testing capacity, poor reporting system and insufficient number of medical staff. The COVID-19 pandemic poses a great threat to most African countries from cities to rural areas and has created a strong demand on already scarce resources and requires an intense mobilization of additional resources to implement established emergency contingency measures. Closure of borders and movements of people restrictions within the country as measures to prevent the spread of COVID-19; this has resulted in the sector being adversely affected by the loss of income. Cooperative prevention and control measures are one of the promising solutions to deplete the spread of COVID-19 on the continent.

• COVID-19 in Africa: status of the pandemic, response and challenges

Nature Medicine. As of 22 May 2020, 54 of 55 African Union (AU) Member States (except Western Sahara) had reported over 100,000 cases and 3,100 deaths. To respond to COVID-19, many AU Member States have been using a combination of containment and mitigation measures. As early as 20 March 2020, AU Member States that had reported fewer than 100 cases were imposing lockdowns and curfews to prevent further COVID-19 transmission within their borders. Probably due to these early efforts, some AU Member States have seen a reduction in average daily case growth. Implementation of the Africa Joint Continental Strategy on COVID-19 will require US\$420 million over the next six months to stop the COVID-19 pandemic. Although several AU Member States and private-sector donors have pledged contributions to the AU COVID-19 response fund, Africa will not be able to meet this demand on its own. International action and solidarity will be needed to beat COVID-19.

Epidemiology Highlights

• Herd immunity and deaths from COVID-19 in Europe

The Lancet: Transmission of SARS-CoV-2 is currently in marked decline in many countries in Europe, North America, and parts of Asia. The observed declines in cases and deaths could be due to the achievement of herd immunity. However, there is little evidence to support that herd immunity is responsible for the decline because there are large differences in patterns of per-capita deaths in different countries that are difficult to reconcile with herd immunity arguments but are easily explained by the timing and stringency of interventions. The herd immunity argument is also at odds with both mortality and seroprevalence data,

• The effect of social distance measures on COVID-19 epidemics in Europe: an interrupted time series analysis

GeroScience: The COVID-19 pandemic recently started declining in Europe following the introduction of unprecedented "stay-at-home" national policies. Our research aims were to characterize the changepoint in the flow of the COVID-19 epidemic in each European country and to evaluate the association of the level of social distancing with the observed decline in the national epidemics. Our findings identified the most probable changepoints in 28 European countries. Before changepoint, incidence of new COVID-19 cases grew by 24% per day on average. From the changepoint, this growth rate was reduced to 0.9%. The beneficial effect of higher social distance quartiles (i.e., turning the increase into decline) was statistically significant for the fourth quartile. Notably, many countries in lower quartiles also achieved a flat epidemic curve. In these countries, other plausible COVID-19 containment measures could contribute to controlling the first wave of the disease. The association of social distance quartiles with viral spread could also be hindered by local bottlenecks in infection control. These results allow for moderate optimism related to the gradual lifting of social distance measures in the general population and call for specific attention to the protection of focal micro-societies enriching high-risk elderly subjects, including nursing homes and chronic care facilities.

• SARS-CoV-2 epidemiological features and SIR modeling of the effect of interventions in India

F1000 Research: A number of steps to limit the spread of the virus in the country have been taken in India including restricted testing, isolation, contact tracing and quarantine, and enforcement of a nation-wide lockdown starting 25 March 2020. A cross-sectional descriptive analysis of the laboratory confirmed COVID-19 patient-wise data collected from a crowdsourced database was completed. The median age of patients was 38 years with 20-39 year-old males being the most affected group. The percent of affected patients who were men was 73.6% (854) and 26.4% (307) were women. A SIR mathematical model estimated between 110,460 – 220,575 infected cases in India at the end of 40 days lockdown if the current contact rate continues.. Interventions have been helpful in preventing the worst-case scenario in India, but will be unable to prevent the spike in number of cases.

Detection of SARS-CoV-2 RNA in fecal specimens of patients with confirmed COVID-19

Journal of Infection: Recent studies show that SARS-CoV-2 RNA may be found in fecal specimens of COVID-19 patients, but the sample size is limited. This systematic review and meta-analysis examined the detection rate of SARS-CoV-2 RNA in fecal specimens of patients according to their clinical characteristics. The pooled detection rate of the RNA was 43.7% by patient and 33.7% by specimens. Females compared to males (59.6% vs. 53.5%), those who presented with gastrointestinal symptoms compared to those without gastrointestinal symptoms (77.1% vs. 57.7%), and patients with severe or critical disease compared to those with mild or moderate disease (68.3% vs. 34.6%) tended to have a higher detection rate. A significant proportion of COVID-19 patients (43.7%) carry SARS-CoV-2 in their intestinal tract. Feces being a self-collected specimen bears a potential to improve case identification in community, especially for young children where proper respiratory sampling at home is difficult. Specific infection control strategies focusing on spread via fecal contamination and faulty toilet drainage are urgently needed.

Global collaborative announced for COVID-19 wastewater-based epidemiology

Environmental Science & Technology: In partnership with the Sewage Analysis CORe group Europe (SCORE) network and the Global Water Pathogen Project, the COVID-19 WBE Collaborative was launched as a hub to coordinate and promote the efforts of research groups undertaking WBE for COVID-19. The website will include content such as press releases,

commentaries, and media content for public outreach and will be used to solicit participation in the collaborative and advertise events relevant to WBE. A workspace is also hosted for rapid informal communication regarding COVID-19 WBE, and plan to host data and protocols for methodological coordination.

Healthcare Policy Recommendations

• A public health approach to the 'lockdown' debate

BMJ Global Health: The current approach to assessing risks and defining interventions in the COVID-19 pandemic takes a narrow medical/epidemiological view. A false dichotomy between saving lives and saving livelihoods has dominated the decision-making on responses to the pandemic. A framework is proposed that includes the major elements of COVID-19-related factors, health systems preparedness, non-COVID-19 medical conditions, social determinants and social protection, with an illustration of its practical application. This, framework provides communities with more agency than one-size-fits-all approaches to COVID-19 control while taking into account human rights, health systems and the SDH.

• NIH's All of Us Program joins fight against COVID-19

National Institutes of Health (NIH) press release: Dr. Francis Collins, Director of NIH, encourages everyone to join All of Us Research Program to assist the scientific community in seeking new insights into COVID-19. The program announced three initiatives including testing blood samples from the initiative's participants, standardization of the rapidly relevant COVID-19 diagnosed information, and deployment of a new online survey to better understand the effects of the pandemic on participants' physical and mental health.

Practice Guidelines

A systematic review of guidelines and recommendations for urology standards of care

European Urology Focus: Of the 15 studied guidelines 14 addressed emergency situations and 12 reported on assessment of elective uro-oncology procedures. There was consensus on postponing radical prostatectomy except for high-risk prostate cancer, and delaying treatment for low-grade bladder cancer, small renal masses up to T2, and stage I seminoma. According to 9 guidelines that addressed endourology, obstructed or infected kidneys should be decompressed, whereas non-obstructing stones and stent removal should be rescheduled. 5 guidelines discussed laparoscopic and robotic surgery, while the remaining recommendations focused on the outpatient procedures and consultations. All recommendations represented expert opinions, with three specifically endorsed by professional societies. Only the European Association of Urology guidelines provided evidence-based levels of evidence (mostly level 3 evidence).

• French recommendations for IBD endoscopy during COVID-19 pandemic

Nature reviews gastroenterology and hepatology: Société Française d'Endoscopie Digestive provides its recommendations. Measures of prevention should be planned and adopted in all endoscopy units that manage patients with and without inflammatory bowel diseases (IBD). In the management of IBD- specific endoscopic situations, alternative biomarkers replacing non-urgent endoscopy, such as fecal calprotectin home test to assess disease activity, should be considered and implemented. To understand whether endoscopy could be rescheduled, it is important to maintain close contact with patients by phone or e-mail to monitor for specific symptoms (through the use of standardized questionnaires) and general clinical condition as well as for indications of SARS- CoV-2 infection.

• The guidelines on convalescent plasma use: differences between high and low-middle income countries

VoxSanguinis: A multidisciplinary, geographically representative group of individuals with expertise spanning transfusion medicine, infectious diseases and hematology has developed the guidance for COVID-19 convalescent plasma (CCP) use. Three subgroups (i.e. donor, product and patient) were established based on self-identified expertise and interest. A series of questions pertaining to each domain was devised and addressed by the subgroups, based on the best available evidence. Here, the donor and product-related challenges are summarized and contrasted between high-income countries (HICs) and low-middle income countries (LMICs). Early challenges in HICs were related to recruitment and qualification of sufficient donors to meet the growing demand. Antibody testing also posed a specific obstacle given the lack of standardization, variable performance of the assays in use and uncertain interpretation of results. In LMICs, an extant transfusion deficit,

suboptimal models of donor recruitment (e.g. reliance on replacement and paid donors), limited laboratory capacity for predonation qualification and operational considerations could impede wide adoption. There has been wide scale adoption of CCP in many HICs, which could increase if the clinical trials show its efficacy. By contrast, LMICs, having received little attention, require locally applicable strategies for adoption of CCP.

Testing

• Patient predictors of risk for positive COVID-19 test: an online risk calculator available

Chest: A prospective registry of 11,672 patients tested for COVID-19 in the Cleveland Clinic was used to investigate whether statistical modeling based on patient characteristics can be used to accurately predict infection with COVID-19. Males, African Americans, older patients, and those with known COVID-19 exposure were at higher risk of being COVID-19 (+). Risk was reduced in those who had pneumococcal polysaccharide or influenza vaccine, or were on melatonin, paroxetine, or carvedilol. The model had favorable discrimination (c-statistic=0.863 in development; 0.840 in validation cohort) and calibration. The authors present sensitivity, specificity, negative predictive value, and positive predictive value at different prediction cut-offs. A calculator for pretest probability of COVID-19 infection is publicly available.

Drugs, Vaccines, Therapies, Clinical Trials

- <u>UK RECOVERY trial finds steroid dexamethasone reduces mortality by 1/3 in severe COVID-19 cases</u>
 - The UK National Institute of Health Research reports in a press release that their RECOVERY trial of dexamethasone shows improved survival rates for ventilated patients with COVID-19 over usual care. A total of 2104 patients were randomized to dexamethasone once per day for ten days and were compared with 4321 patients randomized to usual care alone. Among the usual care control group, 28-day mortality was highest in those on ventilators (41%), intermediate in those on oxygen only (25%), and lowest among those who were not receiving any respiratory intervention (13%). Overall, dexamethasone reduced the risk of 28-day mortality by 17% with a highly significant trend showing greatest benefit among those on ventilators. Mortality was reduced by 1/3 in ventilated patients and by 1/5 in patients receiving oxygen only. No evidence of benefit was found for patients who did not receive oxygen and the study did not include patients outside the hospital setting. Follow-up is complete for over 90% of participants. The trial results are not yet published in a peer-reviewed manuscript.
- The possible pathophysiology mechanism of cytokine storm in elderly adults with COVID-19 infection Inflammation Research: Novel Coronavirus disease 2019 (COVID-19), is an acute respiratory distress syndrome (ARDS). It has proven that COVID-19 infection in some elderly critical adults leads to a cytokine storm, characterized by severe systemic elevation of several pro-inflammatory cytokines. A cytokine storm can induce edematous, ARDS, pneumonia, as well as multiple organ failure in aged patients. It is far from clear till now why cytokine storm induces in only COVID-19 elderly patients, and not in young patients. However, it seems that aging is associated with mild elevated levels of local and systemic pro-inflammatory cytokines, which is characterized by "inflamm-aging". It is highly likely that "inflamm-aging" is correlated to increased risk of a cytokine storm in some critical elderly patients with COVID-19 infection. This review was to summarize experimental data and clinical observations that linked the pathophysiology mechanisms of "inflamm-aging", mild-grade inflammation, and cytokine storm in some elderly adults with severe COVID-19 infection.
- Cancer drug (acalabrutinib) may reduce symptoms of severe COVID-19
 - NIH Research Matters: Hyperinflammatory state in patients with severe COVID-19 is known as a cytokine storm. Cytokines act as chemical messengers that help to stimulate and direct the immune response. But when large amounts of cytokines are released in the body, it can be dangerous. Currently, there are no proven treatment strategies for this phase of the illness. A research team led by Drs. Wyndham H. Wilson, Louis M. Staudt, and Mark Roschewski at NIH's National Cancer Institute (NCI) and Mihalis Lionakis at NIH's National Institute of Allergy and Infection Diseases (NIAID) tested the off-label use of a BTK inhibitor called acalabrutinib to treat COVID-19. They carried out a clinical study of 19 patients with a confirmed COVID-19 diagnosis who required hospitalization and had low blood-oxygen levels and evidence of inflammation. Of these, 11 had been receiving supplemental oxygen for a median of two days, and eight others had been on ventilators for a median of 1.5 days.

48 New COVID-19 Trials registered June 15-16 at clinicaltrials.gov

NIH U.S. National Library of Medicine: Treatment trials of Favipiravir, Pamrevlumab, Pulmozyme, Remdesivir, BAT2020, Lianhua Qingwen, Ivermectin, Ivermectin + Doxycycline, Hydroxychloroquine + Azithromycin, PB1046, Doxycycline, Dipyridamole, Pentoxifylline. At time of writing, a total of 2019 trials were active, 151 completed, and 4 posted results.

Other Science

• High surgical mortality and complications in COVID-19 patients – postpone if possible

JAMA Surgery: In an Italian study, patients with COVID-19 were matched with patients without COVID-19. Of the 123 patients of the combined cohorts (78 women [63.4%]; mean [SD] age, 76.6 [14.4] years), 30-day mortality was significantly higher for those with COVID-19 compared with control patients without COVID-19 (odds ratio [OR], 9.5; 95% CI, 1.77-96.53). Complications were also significantly higher (OR, 4.98; 95% CI, 1.81-16.07); pulmonary complications were the most common (OR, 35.62; 95% CI, 9.34-205.55), but thrombotic complications were also significantly associated with COVID-19 (OR, 13.2; 95% CI, 1.48-infinity). Different models (cumulative link model and classification tree) identified COVID-19 as the main variable associated with complications. The authors conclude that whenever possible, surgery should be postponed in patients with COVID-19.

• Leukocytosis and elevated C-reactive protein can predict worse outcomes: a meta-analysis

Clinica Chimica Acta: Eighteen studies with 3,278 patients were selected. Fever, leukocytosis, and elevated CRP were associated with poor outcomes OR (95% CI) were 1.63 (1.06 to 2.51), 4.51 (2.53 to 8.04), and 11.97 (4.97 to 28.8), respectively. Leukopenia was associated with a better prognosis (OR 0.56, 95% CI 0.40 to 0.78). Sensitivity analyses showed similar tendencies. Meta-regression analysis for leukocytosis indicated that age, dyspnea, and hypertension contributed to heterogeneity.

Neurological manifestations of COVID-19

Journal of Neurology: A meta-analysis of 41 studies for prevalence of nine neurologic COVID-19 manifestations in 3837 patients revealed that the most common manifestations were fatigue (33.2% [23.1-43.3]), anorexia (30.0% [23.2-36.9]), dyspnea/shortness of breath (26.9% [19.2-34.6]), and malaise (26.7% [13.3-40.1]). The common specific neurological symptoms included olfactory (35.7-85.6%) and gustatory (33.3-88.8%) disorders, especially in mild cases. Guillain-Barre syndrome and acute inflammation of the brain, spinal cord, and meninges were repeatedly reported after COVID-19. Laboratory, electrophysiological, radiological, and pathological evidence supported neurologic involvement of COVID-19.

• Thromboembolic risks in patients with COVID-19

Pan African Medical Journal: COVID-19 pandemic is an emergent cardiovascular risk factor and a major cause of mortality worldwide. Thromboembolism is highly suspected as a leading cause of death in these patients through vascular inflammation caused by SARS COV2. Until now there is no real treatment of COVID-19 and many proposed drugs are under clinical trials. Considering the high incidence of thromboembolic events in critically ill patients with COVID-19, prevention of this disorder should be essential in order to reduce mortality in these patients.

• Animals can be reservoir for MERS-CoV and SARS-CoV infections: a meta-analysis

Infez Med: From a total of 34 studies (n=20,896 animals), the pool prevalence by RT-PCR for MERS-CoV was 7.2% (95%CI 5.6-8.7%), with 97.3% occurring in camels, in which pool prevalence was 10.3% (95%CI 8.3-12.3). Qatar was the country with the highest MERS-CoV RT-PCR pool prevalence: 32.6% (95%CI 4.8-60.4%). From 5 studies and 2,618 animals, for SARS-CoV, the RT-PCR pool prevalence was 2.3% (95%CI 1.3-3.3). Of those, 38.35% were reported on bats, in which the pool prevalence was 14.1% (95%CI0.0-44.6%). Thus, a considerable proportion of infected animals tested positive, particularly by nucleic acid amplification tests (NAAT). Camels and bats were found to be positive by RT-PCR in over 10% of the cases for both; thus, suggesting their relevance in the maintenance of wild zoonotic transmission.

• Risk of hepatic failure in COVID-19 patients

Infez Med: A total of 4191 COVID-19 patients were included in the meta-analysis. The pooled prevalence of liver injury was 19.5% (95% CI: 14.3-26.1). There was significant heterogeneity among the 19 studies (X2 = 738.5; p < 0.001; I2 = 94.34%). Among 288 death cases, the pooled prevalence of liver injury was 22.8% (95% CI: 11.7-39.8). In summary, the COVID-19

disease itself can result in severe and even fatal respiratory diseases and even may lead to ARDS and multiple organ failure. The results of this systematic review highlight the importance of liver injury that may assist clinicians anywhere in the globe in controlling COVID-19-related infection and complications. Moreover, the prevalence of liver injury can be higher in severe cases than in mild cases.

• A review of cardiac complications in COVID-19

Cureus: SARS-CoV-2 infection has shown an association with acute myocardial injury, cardiomyopathy, and myocarditis. Virus-related myocardial injury is associated with inflammation, impairment of cardiac function, and malignant ventricular tachyarrhythmias. When COVID-19 is complicated by acute myocardial injury, a significant increase in mortality occurs. The authors urge physician awareness of the elevated morbidity and mortality of myocardial involvement in COVID-19. They anticipate that, because of the high inflammatory response, other cardiovascular complications may also occur in COVID-19 patients with severe symptoms.

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