6-18-2020

2020-06-17/18 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

Lori D. Sloane

Mari Anixter

See next page for additional authors

Authors

Christophe G. Lambert, Shawn Stoicu, Ingrid Hendrix, Lori D. Sloane, Mari Anixter, Anastasiya Nestsiarovich, Praveen Kumar, Morgan Edwards-Fligner, Emma Wolinsky, Alexandra Yingling, Kristine Tollestrup, Orrin Myers, and Douglas J. Perkins

DAILY UNM GLOBAL HEALTH COVID-19 BRIEFING

June 17-18, 2020

Executive Summary

NM Highlights: NM case count. UNM housing plan for fall 2020. Navajo Nation health and social inequities.

US Highlights: Banning airline passengers.

Economics, Workforce, Supply Chain, PPE: COVID-19 Exit Strategy. Effect of extended use respirators and PPE.

Epidemiology Highlights: Model predicts effects of strategies on US epidemic. Index for assessing risk of contagion.

Practice Guidelines: Institutional antithrombotic protocols in US and France are reviewed. Shortcomings of restricted hospital visitation are discussed.

Testing: Current testing strategies and assays. Reducing transmission in incarcerated populations.

Drugs, Vaccines, Therapies, Clinical Trials: More detail on dexamethasone trial. Methylprednisolone improved outcomes. Outcomes on ACEI/ARB. 34 new trials.

Other Science: Nearly 20% of world's population is at risk for severe disease. High-flow nasal cannula for acute respiratory failure. Genome-wide association study of patients with severe disease. Frail geriatric COVID-19 patients have a higher risk of delirium. Asymptomatic infection is associated with a longer virus shedding and a weaker immune response.

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

- NM reports 4 more COVID-19 deaths and 94 additional cases on June 18

  As of today (6/18), the total positive cases and total deaths in the state are 10,153 and 456, respectively. The state has performed 275,897 tests, there are 157 individuals currently hospitalized for COVID-19, and 4,217 COVID-19 cases have recovered. NMDOH portal featuring epidemiologic breakdown of cases.

- UNM plans for on-campus housing for fall 2020

  KRQE: UNM announced a plan to bring back on-campus living for students enrolled in Fall 2020 classes, which includes single-occupancy-only dorm rooms, and having residents agree to social distancing and risk of COVID-19. Priority for living space will be given to freshmen and those who applied for priority renewal. UNM will still require freshmen to buy meal plans, which will be distributed as to-go meals and grub hub deliveries if the state ban on buffets and salad bars is still in effect.

- A UNM physician treating patients in the hard-hit Navajo nation highlights health and social inequities

  U.S.News: The Navajo Nation, home to about 174,000 people as of the last census, has become the epicenter of the novel

coronavirus in the country. As of June 8, the reservation reported 6,110 cases of COVID-19 and 277 deaths – up from 148 cases and five deaths in late March. By mid-May, the Navajo Nation had exceeded New York and New Jersey for the highest per-capita coronavirus infection rate in the U.S. Experts attribute the startling transmission rates in the Navajo Nation to health and social inequities, such as a lack of paved roads, inadequate access to running water, high rates of children living in poverty, underfunded health services.

US Highlights

- Major U.S. airlines may ban passengers who refuse to wear masks

  Airlines may prevent anyone not wearing a mask from boarding and will provide the coverings to passengers who have none. Passengers will be informed about the airline's policy on face coverings prior to boarding and onboard. Each airline will decide the appropriate consequences for passengers failing to comply, which may include being put on the airline's no-fly list.

Economics, Workforce, Supply Chain, PPE Highlights

- Unlocking towns and cities: COVID-19 exit strategy (Commentary)

  Eastern Mediterranean Health Journal (EMHJ): The UK (and WHO) authors discuss the strategies to unlock towns and cities. While some countries are reporting a decline in new COVID-19 cases, many others are yet to feel the full impact of the virus. Authors draw the conclusion: Maintaining current aggressive social distancing measures until an effective treatment or vaccine are available, is not practical. Gradually relaxing restrictions when infection indicators (decreased trans-mission and spread of the virus) and other conditions are met, could help further easing of measures until the authorities are sure that no new cases are reported for a reasonable length of time. Governments must ensure that their unlocking plan can be implemented in practice, clearly communicated and enforced.

- Effect of extended use N95 respirators and eye protection on PPE utilization (Letter to Editor)

  Antimicrobial Resistance & Infection Control: Prior to 4 February 2020, N95 respirators and eye protection were single-patient use in Singapore. On 4 February, reusable goggles were issued to each HCW. On 8 February, a directive was issued recommending extended use of N95respirators and eye protection for repeated encounters with different patients, without changing between patients unless visibly contaminated or dislodged (Supplementary Appendix Floor Plan). Gowns and gloves remained as single-patient use. During study period, a daily ward-level stock take calculating the difference in balance PPE compared to preceding day, accounting for supplies replenished, was defined as utilization rate per day. A daily ward census was recorded. A total of 77 confirmed and 725 suspect cases were admitted during study period. During the COVID-19 pandemic, the average utilization rate of single-use eye and N95 respirators per 100 patient-days reduced as a result of extended use policy. The average utilization rate of single-use eye protection and N95 respirators reduced from 1950 to 250 and 2490 to 1710 respectively after implementation. Before extended usage, the N95 respirator utilization per 100 patient-days steadily increased from 400 on 1February to 5428.6 on 8 February (β= 521.22) (Supplementary Appendix Fig. A). After implementation, theN95 utilization rate dropped to 388.1 on 2 March (β=11.04). Single–use eye protection utilization rate per 100patient-days was 2076.3 on 1 February and had de-creased to 1411.4 on 3 February (β=−332.45) By 2 March, it decreased sharply to 32.84 (β= 4.84).

Epidemiology Highlights

- Model predicts effect of strategies on the COVID-19 epidemic in the US

  J of Macroeconomics: An extended SIR model with agents optimally choosing outdoor activities was created. The model was calibrated and matched to the data from the United States. The model predicts the epidemic in the United States very well. Without government intervention, the simulation shows that the epidemic peaks on 22 March, 2020 and ends on 29 August, 2022. By the end of the epidemic, more than 21 million people will be infected, and the death toll is close to 3.8 million. The model predicts that no single policy can effectively suppress the epidemic, and the most effective policy is a hybrid policy with lockdown and broadening testing. Lockdown policy alone is ineffective in controlling the epidemic as agents would have optimally stayed at home anyway if the infection risk is high even without a lockdown. Broadening testing solely will

accelerate the return to normal life as there are fewer infected people hanging around. However, as people do not internalize the social costs of returning to normal life, the epidemic could get even worse. Increasing medical capacity without any other measures only has temporary effects on reducing the death toll. Random testing is too inefficient unless a majority of population is infected.

- An index to predict risk of contagion in urban district lockdown

  Safety Science: An index was developed to predict the risk of contagion in urban districts to support government administrations in identifying the best strategies to reduce or restart local activities during lockdown conditions. The index considers socio-economic data such as the presence of activities, companies, institutions and number of infections in urban districts. The proposed index is based on a factorial formula, is simple and easy to apply by practitioners, and is calibrated by using an optimization-based procedure using data from 257 urban districts of the Apulian region (Italy). The index is compared with a more refined analysis based on the training of Artificial Neural Networks which takes into account the non-linearity of the phenomenon. The investigation quantifies the influence of each parameter in the risk of contagion.

Practice Guidelines

- Institutional antithrombotic protocols for COVID-2019

  Research and practice in thrombosis and haemostasis: The authors compare different institutional protocols proposed in US and France. Here are their summary recommendations: Medical floor COVID-19–positive patients: use LMWH (low molecular weight heparin) at prophylactic or intermediate doses as the preferred agent over unfractionated heparin (UFH), unless patients have severe renal insufficiency. Patients with severe COVID-19 requiring high-flow oxygen or ventilator: use LMWH at prophylactic or intermediate doses as the preferred agent over UFH in ICU settings, with serious illness meeting sepsis-induced coagulopathy score of ≥4 or with markedly elevated D-dimer (>6× ULN). Extended thromboprophylaxis: Patients hospitalized with COVID-19, especially those with an IMPROVE VTE score of ≥4, elevated D-dimer (>2× ULN), or over 60 years and without bleeding risk factors, or recent ICU stay should be strongly considered for extended thromboprophylaxis up to 40 days after hospital discharge with either lovenox 40 mg s.c. daily, rivaroxaban 10 mg p.o. daily, or betrixaban 80 mg p.o. daily. Routine empiric therapeutic dose of intravenous UFH or systemic tissue plasminogen activator or routine use of inferior vena cava filters: No current supporting evidence for its use without absolute indications. Continuation of home antithrombotic medications or need of chronic antithrombotic: Patients on antiplatelets or oral anticoagulants (OACs) should be kept on their therapy unless there are absolute contraindications (such as active bleeding, severe thrombocytopenia, planned procedure, or significant new drug interaction or other contraindications). DOACs are preferred over warfarin for treatment of VTE or atrial fibrillation due to decreased need for monitoring. Lopinavir/ritonavir may potentiate CYP3A4 or P-gp inhibition, and as such there may be reduction in clopidogrel effects and increased effects of ticagrelor – thus, switch them over to prasugrel if possible or consider platelet function studies (P2Y12 monitoring). For OACs, if possible, patients may be switched to dabigatran, edoxaban, or betrixaban from apixaban and rivaroxaban as the DOACs of choice if combined therapy with CYP3A4 inhibitor is prescribed. Alternatively, dose-adjusted warfarin with frequent INR monitoring should be a good option.

- The shortcomings of restricted hospital visitation

  Pediatric Critical Care Medicine: The authors from the University of Michigan Medical Center warn that severely restricted visitation policies undermine our ability to provide humane, family-centered care, particularly during critical illness and at the end of life. The enforcement of these policies consequently increases the risk of moral distress and injury for providers. The authors surveyed the shortcomings of current visitation restrictions. They argue that hospital visitation restrictions can be implemented in ways that are nonmaleficent, but this requires unwavering acknowledgment of the value of social and familial support during illness and death. They advocate that visitation restriction policies be implemented by independent, medically knowledgeable decision-making bodies, with the informed participation of patients and their families.

Testing

- Review of currently available COVID-19 testing

  AAS Open Research: Diagnostic tests were developed rapidly for COVID-19, but there is still need for the development of rapid and specific point-of-care testing. This review outlines different approaches to testing and compares the available test assays including the Xpert(R) Xpress SARS-CoV-2 test (takes ~45 min) and Abbott ID COVID-19 test (5 min). These assays are the point-of-care tests for diagnosis of novel COVID-19 that have so far received the US Food and Drug Administration emergency use authorizations clearance. Improving both the rapidity and sensitivity of testing is key to efforts to contain the virus.

- Effectiveness of various strategies to reduce transmissions in jails and prisons

  MedRxiv preprint: COVID-19 presents a serious health risk to the incarcerated population. Depopulation, single occupancy of cells, and asymptomatic testing can be effective strategies to mitigate transmission in these settings when added to standard public health measures. Coordination of health care and social services organizations prior to release should be prioritized, as should testing. The large estimated reduction in the transmission rate (≥ 50%) from these three strategies is comparable to standard social distancing measures in a community setting.

Drugs, Vaccines, Therapies, Clinical Trials

- Further details on the UK RECOVERY dexamethasone trial

  Oxford University press release: While the results on the UK RECOVERY trial on the steroid dexamethasone are yet to be published, it was halted by the Steering Committee because sufficient patients had been enrolled to establish benefit. The trial web site reported on the effect sizes and their statistical significance. Dexamethasone (6 mg/d for 10 days) reduced deaths by one-third in ventilated patients (rate ratio 0.65 [95% confidence interval 0.48 to 0.88]; p=0.0003) and by one fifth in other patients receiving oxygen only (0.80 [0.67 to 0.96]; p=0.0021). There was no benefit among those patients who did not require respiratory support (1.22 [0.86 to 1.75]; p=0.14).

- Methylprednisolone improves outcomes in hospitalized patients with CoVID-19 pneumonia

  MedRxiv preprint: A small controlled trial (n = 85) of a short course of methylprednisolone showed improvement of the composite endpoint of death, ICU admission or requirement of non-invasive ventilation. MP was associated with a reduced risk of the composite endpoint in the intention-to-treat, age-stratified analysis (combined risk ratio 0.55 [95% CI 0.33-0.91]; p=0.024). A decrease in C-reactive protein levels was more pronounced in the MP group (p=0.0003). Hyperglycemia was more frequent in the MP group.

- Outcomes on angiotensin-converting enzyme inhibitors/angiotensin receptor blockers: a meta-analysis

  European Heart Journal - Cardiovascular Pharmacotherapy: Review of 16 studies showed conflicting findings on severity and mortality in patients taking these drugs. In a pooled analysis of four studies, there was a non-significant association of ACEI/ARB use with lower odds of developing severe disease vs. non-users [OR = 0.81, 95% CI: 0.41-1.58, I2=50.52, P= 0.53). In a pooled analysis of 6 studies, there was a non-significant association of ACEI/ARB use with lower odds of mortality as compared with non-users (OR = 0.86, 95% CI = 0.53-1.41, I2 = 79.12, P = 0.55). It is concluded that ACEIs and ARBs should be continued in COVID-19 patients, reinforcing the recommendations made by several medical societies. Additionally, the individual patient factors such as ACE2 polymorphisms which might confer higher risk of adverse outcomes need to be evaluated further.

- 34 New COVID-19 Trials registered June 17-18 at clinicaltrials.gov

  Treatment trials: Hydroxychloroquine, Crizanlizumab, Opaganib, Ivermectin, Tocilizumab, Nitazoxanide, Ciclesonide, Camostat Mesylate, Microcrystalline Cellulose, Maraviroc, Niclosamide, ketotifen1. At time of writing, a total of 2043 were active, 161 completed, and 4 posted results.

Other Science

- Almost 20% of world's population has at least one underlying condition raising risk of severe COVID-19

  Lancet: UK authors estimated the number of individuals at increased risk of severe disease by age, sex, and country for 188 countries. It was estimated that 1·7 billion people, comprising 22% of the global population, have at least one underlying condition that puts them at increased risk of severe COVID-19 if infected (ranging from <5% of those younger than 20 years to >66% of those aged 70 years or older). It was estimated that 349 million (186–787) people (4% [3–9] of the global population) are at high risk of severe COVID-19 and would require hospital admission if infected (ranging from <1% of those younger than 20 years to approximately 20% of those aged 70 years or older). It was also estimated that 6% of males are at high risk compared with 3% of females.

- High-flow nasal cannula for acute hypoxemic respiratory failure in COVID-19: systematic reviews

  Canadian Journal of Anesthesia: The authors conducted two WHO-commissioned reviews to inform use of high-flow nasal cannula (HFNC) in patients with COVID-19. They synthesized the evidence regarding efficacy and safety (review 1), as well as risks of droplet dispersion, aerosol generation, and associated transmission (review 2) of viral products. No eligible studies included COVID-19 patients. Review 1: 12 RCTs (n = 1,989 patients) provided low-certainty evidence that HFNC may reduce invasive ventilation (relative risk [RR], 0.85; 95% confidence interval [CI], 0.74 to 0.99) and escalation of oxygen therapy (RR, 0.71; 95% CI, 0.51 to 0.98) in patients with respiratory failure. Results provided no support for differences in mortality (moderate certainty), or in-hospital or intensive care length of stay (moderate and low certainty, respectively). Review 2: 4 studies evaluating droplet dispersion and three evaluating aerosol generation and dispersion provided very low certainty evidence. Two simulation studies and a crossover study showed mixed findings regarding the effect of HFNC on droplet dispersion. Although two simulation studies reported no associated increase in aerosol dispersion, one reported that higher flow rates were associated with increased regions of aerosol density. Thus, high-flow nasal cannula may reduce the need for invasive ventilation and escalation of therapy compared with conventional oxygen therapy in COVID-19 patients with acute hypoxemic respiratory failure. This benefit must be balanced against the unknown risk of airborne transmission.

- Genome wide association study of severe Covid-19 with respiratory failure COVID19

  NEJM: The authors conducted a genome wide association study involving 1980 patients with Covid-19 and severe disease (defined as respiratory failure) in Italy and Spain. They analyzed 8,582,968 single-nucleotide polymorphisms and conducted a meta-analysis of the two case-control panels. They detected cross-replicating associations with rs11385942 at locus 3p21.31 and with rs657152 at locus 9q34.2, which were significant at the genome wide level (P<5×10−8) in the meta-analysis of the two case–control panels (OR= 1.77; 95% CI, 1.48 to 2.11; p=1.15×10−10; and OR= 1.32; 95% CI, 1.20 to 1.47; p=4.95×10−8, respectively). At locus 3p21.31, the association signal spanned the genes SLC6A20, LZTFL1, CCR9, FYCO1, CXCR6 and XCR1. The association signal at locus 9q34.2 coincided with the ABO blood group locus; in this cohort, a blood-group–specific analysis showed a higher risk in blood group A than in other blood groups (odds ratio, 1.45; 95% CI, 1.20 to 1.75; P=1.48×10−4) and a protective effect in blood group O as compared with other blood groups (odds ratio, 0.65; 95% CI, 0.53 to 0.79; P=1.06×10−5).

- Frailty predicts delirium in elderly hospital and community population with COVID-19

  MedRxiv preprint: In this observational study two UK cohorts over 65 yo were explored: hospital cohort (N=322 with confirmed COVID-19) and community cohort (N=535 reported test-positive for COVID-19). In Hospital cohort, after age-matching, delirium was reported in 40 (38%) of frail and 13 (12%) of non-frail patients. Frailty was found to significantly predict delirium (P=0.013; OR 95% CI = 3.22 (1.44, 7.21)). There were no significant differences between frail and not frail for other symptoms (fever (temperature ≥ 37.5C) and cough). In community cohort, after age-matching, frailty was found to significantly predict delirium (P=0.038; OR (95% CI) = 2.29 (1.33, 4.00)), after FDR correction for multiple testing. Frailty also predicted fatigue (P-value: 0.038; OR = 2.23 (1.27, 3.96)) and shortness of breath (P-value: 0.043; OR = 2.00 (1.19, 3.39)). There were no significant differences between frail and not frail for the other 11 symptoms analyzed. Systematic frailty assessment and screening for delirium in acutely ill older patients in hospital and community settings is needed. Clinicians should suspect COVID-19 in frail adults with delirium.

- Asymptomatic individuals with SARS-CoV-2 have a longer shedding and weaker immune response

  Nature Medicine: The authors studied 37 asymptomatic individuals in China with SARS-CoV-2 in the preceding 14 days and

during hospitalization. The median duration of viral shedding in the asymptomatic group was 19 days (interquartile range (IQR), 15–26 d). The asymptomatic group had a significantly longer duration of viral shedding than the symptomatic group (log-rank P= 0.028). The virus-specific IgG levels in the asymptomatic group (median S/CO, 3.4; IQR, 1.6–10.7) were significantly lower (P= 0.005) relative to the symptomatic group (median S/CO, 20.5; IQR, 5.8–38.2) in the acute phase. Of asymptomatic individuals, 93.3% (28/30) and 81.1% (30/37) had reduction in IgG and neutralizing antibody levels, respectively, during the early convalescent phase, as compared to 96.8% (30/31) and 62.2% (23/37) of symptomatic patients. 40% of asymptomatic individuals became seronegative and 12.9% of the symptomatic group became negative for IgG in the early convalescent phase. Asymptomatic individuals had lower levels of 18 pro- and anti-inflammatory cytokines.

Contributing team members: Christophe G. Lambert, Shawn Stoicu, Ingrid Hendrix, Lori Sloane, Mari Anixter, Anastasiya Nestsiarovich, Praveen Kumar, Nicolas Lauve, Morgan Edwards-Fligner, Emma Wolinsky, Alexandra Yingling, Kristine Tollestrup, Orrin Myers, Douglas J. Perkins.