This weekly science review is a snapshot of the new and emerging scientific evidence related to COVID-19 during the period specified. It is a review of important topics and articles, not a guide for policy or program implementation. The findings captured are subject to change as new information is made available. We welcome comments and feedback at covid19-eiu@vitalstrategies.org.

DATA INSIGHT:

**Country preparedness and COVID-19**

An obvious question is whether the preparedness level of a country has made a difference in the current COVID-19 pandemic. Do countries that score higher on preparedness for more common outbreaks and epidemics perform better in the current pandemic? The relationship between preparedness and COVID-19 impact is difficult to answer, as both are complex and hard to measure. In this insight, we used simple metrics for each to see if any patterns emerged.

**Preparedness and key indicators**

We selected 29 countries that represent more than 2.2 billion people (28% of global total), more than 1.3 million COVID-19 cases (41%) and more than 78,000 COVID-19 deaths (33%) as of 1 May 2020. The preparedness levels of these 29 countries vary greatly. We then charted some key indicators by ReadyScore country to better describe the data. These are simple correlations of national-level data, subject to the
typical limitations of using this type of data. It is important to note that national level measures do not capture important sub-national trends.

Summary

Some key observations can be made when examining the relationship between preparedness and some key COVID-19 indicators. Better prepared countries tended to be older and test more of their population. They also had higher CFRs, but lower than expected given the proportion of older people in their populations. This indicates that countries that are better prepared do a better job finding cases and preventing deaths. Better prepared countries did not act sooner to implement PHSMs, and more information is needed to better understand this relationship at country level, including other factors that influenced decision-making.

IN-DEPTH TOPICS

Stroke, thrombotic, and thromboembolic events in COVID-19 patients

Large-vessel occlusion (LVO) refers to a type of ischemic stroke in which blood flow to a large portion of the brain is cut off due to a clot or ruptured plaque that usually originated elsewhere, such as in the heart or a more proximal larger artery. LVOs are important due to their disproportionate ability to result in disability, morbidity and mortality compared to other ischemic strokes. They typically affect men and women equally at an average age of 63 to 70 years. Patients who experience LVOs have high rates of comorbidities such as atrial fibrillation and irregular heart rate, high blood pressure, diabetes, and tobacco use.

Recently, there have been reports of people outside this typical profile presenting with LVOs while experiencing COVID-19 infection. An article in the New England Journal of Medicine described one hospital’s experience with five COVID-19 patients under the age of 50, most without any known risk factors for stroke, presenting with devastating stroke.
These large vessel strokes may be one manifestation of a more general process affecting COVID-19 patients. Overall, COVID-19 patients, especially those with severe disease, appear to have thrombotic complications (problems with clots) and thromboembolic complications (problems with clots starting in one place and traveling elsewhere) in higher numbers than other hospitalized or critically ill patients. These events affect both arteries and veins. Such complications can include clots in arteries traveling to other organs or limbs or clots forming in the deep veins such as in the legs and traveling to the lungs where they can cause additional problems oxygenating blood adequately and straining the heart.

There is some experience with critical illness in general, and prior novel coronaviruses, that can shed light on what may be driving these types of complications. Notably, LVOs and other thrombotic and thromboembolic complications were described during the SARS epidemic in 2002-2003. SARS-CoV-2 infection most commonly affects the lungs, although it can affect many parts of the body. Inside the cells that line the body's blood vessels from the largest arteries and veins to the smallest capillaries, COVID-19 causes changes—possibly as a result of the virus itself or the immune system's response—that may be causing irregularities in the body's tendency to form clots and break them down properly. Researchers have even suggested that these pathways of abnormal coagulation may be one aspect of the most severe respiratory failure in COVID-19 patients. In other cases, clinicians have noted outcomes such as COVID-toe, a delayed seemingly benign complication that maybe related to immune reaction or tiny clots in small vessels.

Researchers continue to look at both the biochemical changes in the bloodstream, such as the activity of clotting factors, changes in platelet number and function, and how quickly or effectively the body can create or break down a clot when needed. Researchers are also looking at how these factors relate to patients who are suffering from clot related complications and more severe disease. A recent review in the Journal of the American College of Cardiology presents the work of a number of collaborators from around the world, including China, Italy and the US, and discusses the emerging body of evidence on thrombotic and thromboembolic events in COVID-19 patients, their sequelae, and implications.
A better understanding of the pathways involved in thrombotic and thromboembolic complications in COVID-19 is necessary. It can provide us with the opportunity to augment guidelines for risk-stratification and prevention of blood clots in some COVID-19 patients, and to pay closer attention to possible treatments that may interfere with clotting and blood thinning. This area of research is advancing our overall understanding of how the virus interacts with the body and its immune system to cause disease, and can shed light on how to better care for patients and prevent complications.

**COVID-19 in correctional facilities and homeless shelters**

Allocation of limited COVID-19 testing resources can be guided by identifying populations that are high priority for testing. Testing for COVID-19 is especially critical if confirming infections may improve clinical outcomes or reduce the spread of disease. According to these parameters, those who live in congregate facilities, including persons experiencing homelessness and those in correctional institutions, should be prioritized for testing.

The United States has the highest incarceration rate in the world, with more than 2 million people living in correctional facilities. Inmates have higher rates of chronic diseases, including HIV, than the general population. In addition, the proportion of the inmate population over 55 has grown. States vary in their approaches to testing for COVID-19 in correctional settings. New York and Ohio each have approximately 50,000 federal and state inmates. In New York, which utilizes symptom-based testing protocols, there have been 391 confirmed cases among inmates and 1095 cases among staff. Ten inmates and two staff members have died from COVID-19 as of May 2. Ohio has expanded testing within correctional institutions and has confirmed nearly 4,000 cases, or approximately one-quarter of the state’s cases, among inmates. Several correctional institutions have been in the news for high COVID-19 prevalence rates after expanding testing. At the Marion Correctional Institution in Ohio, more than 2,000 cases have been confirmed among 2,500 inmates. Five inmates and one guard have died. At Cook County Jail in Chicago, Illinois, there have been more than 400 cases identified among approximately 1,000 inmates tested; six have died. High proportions of cases are reported to be asymptomatic. According to Reuters, prison records and interviews...
with prison officials revealed that in four states conducting expanded testing (Arkansas, North Carolina, Ohio and Virginia), 96% of 3,277 inmates who tested positive for SARS-CoV-2 were asymptomatic.

Some have compared correctional facilities to the cruise and naval ships on which there have been COVID-19 outbreaks, but a major different is that staff from correctional institutions regularly go between their work environment and the general community. In most states, testing of staff members occurs in the community just as for the rest of the general public. In Ohio, which is conducting universal testing among correctional institution staff at some institutions, more than 440 cases have been confirmed among staff members as of May 2. Per news reports, among Michigan’s 12,000 corrections department staffers, 210 have tested positive for SARS-CoV-2 and two have died. A number of cases in the community have been linked to outbreaks in correctional institutions, including 66 cases in Marion County, Ohio linked to the Marion Correctional Institution.

Each night in the United States, more than 500,000 people experience homelessness, and over half of those individuals stay in shelters. Among the homeless, many are elderly and the prevalence of a range of communicable and noncommunicable diseases is higher than in the general population. Results of COVID-19 testing in 19 homeless shelters (1,192 residents and 313 staff members) showed that high proportions of residents and staff were PCR-positive for SARS-CoV-2 in shelters where multiple COVID-19 cases had been reported. For example, in three Seattle shelters with known case clusters, 17% of residents and 17% of staff members tested positive; in 12 Seattle shelters where only one case had been identified, 5% of residents and 1% of staff members tested positive. The authors suggested testing of all residents and staff before clusters are identified and regardless of symptoms. Indeed, a study conducted in a Boston shelter showed that of 408 study participants, 147 (36%) were PCR-positive for SARS-CoV-2 and 88% of those were asymptomatic.

Recommendations for limiting disease spread within shelters and correctional facilities include physical distancing for all, and segregation of people on the basis of screening for fever and other symptoms or viral test results. Among the homeless population, efforts are being made to expand testing to asymptomatic individuals and to house COVID-19 patients separately from others. There are efforts to
separate inmates with medical comorbidities, and there has been some reduction in over-crowding of prisons through early release of inmates. In order to reduce epidemic spread among the millions who continue to live in congregate facilities, many of whom are at higher risk for severe disease and mortality due to age or underlying comorbidities, universal testing for those in congregate facilities should be prioritized. In addition, to protect those who work in congregate facilities and to prevent epidemic spread into surrounding communities, prioritization of testing for staff members at congregate facilities should be considered and measures to reduce the size and crowding of these populations should be implemented.

Relaxing public health and social measures in the United States

States across the US are beginning to reopen. By May 4th, half of US states will have taken steps to lift restrictions on non-essential businesses and other activities. In many cases, reopening doesn’t apply to the whole state, either because mayors and county executives have maintained stronger restrictions or because governors have excluded harder-hit parts of the state from the first stages of reopening.

Reopening is not happening all at once—most states are following a phased process. In the first phase, only a few types of non-essential businesses are allowed to operate, often with restrictions to promote continued physical distancing. For instance, in Tennessee, retail and restaurant employees must wear masks and gloves at all times and the establishments can only hold 50% or less of their usual capacity. The types of businesses allowed to open varies widely across states (Table 1). In Minnesota, only offices and other industries that are not consumer-facing are allowed to open, but in Georgia the focus is mostly on reopening consumer-facing businesses such as retail, beauty salons, and even movie theaters.

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**Table 1: Loosening of restrictions by state**

*Date represents the first date that restrictions were loosened.

**Many of these businesses or venues are opening with physical distancing restrictions in places.

Some states that are reopening, such Montana and Alaska, appear to have their epidemic largely under control with evidence of declining cases and sufficient testing, according to criteria suggested by one group. At least seven states are beginning to reopen despite experiencing an increase in cases (Tennessee, Colorado, Indiana, Iowa,
Kansas, Minnesota and Wyoming). Other states where cases appear to be declining, such as Florida and Georgia, still have large gaps in testing and may be missing many cases. One state, Mississippi, halted a planned May 4th expansion of its reopening after seeing the highest number of cases and deaths in a single day on May 1.

In April, the White House released guidelines to help states decide when to reopen. States should meet criteria on symptoms (two-week downward trend in reported symptoms for both influenza-like illness and COVID-like illness), cases (two week downward trend in cases reported or the percent of tests that are positive), and hospitals (sufficient hospital capacity for all current COVID-19 patients and a testing program in place for at-risk healthcare workers). Resolve to Save Lives’ draft guidance for reopening also includes criteria for contract tracing, testing, and isolation of COVID-infected individuals. Although many of the public health factors that should go into the decision to reopen are not easily measurable or accessible to the public, it is clear that many states do not yet meet even basic standards of declining case counts and sufficient testing.

In this context, “open” and “closed” are not dichotomous. Even at times when physical distancing is widely recommended, health care, essential services, and many activities of society continue. Analogously, even when societies begin to loosen physical distancing restrictions, there will be many activities which cannot be resumed safely unless it is confirmed that the virus is no longer circulating (e.g., choir practice and certain mass gatherings).

Looking forward, it will be important to understand the impact of reopening. Mobility data can provide objective measures of physical distancing. Trends in new cases, testing, symptoms, and (if available) in syndromic surveillance markers such as influenza-like illness will also be critical to monitor in the near future. If loosening restrictions leads to sharp increases in cases or other warning signs, there may be a need to reimpose more stringent measures.

**Remdesivir**

*Remdesivir* is an antiviral medication created as a treatment for diseases caused by the Ebola and Marburg viruses. Several studies are currently evaluating its effectiveness as a treatment for COVID-19, and
this week a few initial results were reported. First, a Lancet article was published on a multi-site randomized placebo controlled trial of remdesivir for severe COVID-19 pneumonia in Wuhan, China. The results showed no statistically significant impact on viral load nor in time to clinical improvement overall. However, there was a nonsignificant trend toward faster clinical improvement in remdesivir-treated patients when treatment was started within 10 days of symptom onset. Although well-designed, conducted and reported, the study had limited statistical power, especially for the subgroup analysis. Enrollment was curtailed after recruiting just over half the intended sample size (n=237 of a planned 453) before the local epidemic was controlled in mid-March and additional eligible patients could not be found. Second, Gilead Sciences, the company which manufactures remdesivir, announced that in a Phase 3 trial of the medication in patients with severe COVID-19, similar improvements in clinical course were found in those taking a five-day treatment course as those receiving a ten day treatment course. This is important in that more people can potentially be treated with remdesivir if the duration of effective treatment is shorter. Full data on this trial has not yet been made available. Last, the US National Institutes of Health announced that in an ongoing randomized controlled trial of about 1,000 hospitalized COVID-19 patients with lung involvement, remdesivir accelerated recovery from COVID-19. The median time to recovery was 11 days for patients treated with remdesivir, compared to 15 days for patients who received placebo (p<0.001) There was also a non-significant trend toward a survival benefit, with 8% mortality in the remdesivir group versus 11.6% mortality in the placebo group (p=0.059). These are preliminary results from an ongoing clinical trial, and the full data are not expected until late May.

Overall, there is promising evidence from well-designed clinical trials that suggests that remdesivir is effective at reducing the duration of COVID-19 illness. On May 1, the US Food and Drug Administration issued an Emergency Use Authorization for remdesivir treatment in adults and children hospitalized for severe COVID-19 disease. More evidence on remdesivir is coming soon and will be needed to fully ascertain the benefits and risks of treatment. Even if proven effective, this is not a silver-bullet treatment or cure, but rather an exciting development as the first medication that shows promise against COVID-19 disease in humans and a potential means to reduce the burden on hospitals and improve patient outcomes.
Out-of-Hospital Cardiac Arrest during the Covid-19 Outbreak in Italy

(NEJM, 29 April 2020)

Main message: In the Lombardy Region of Italy, data suggests an association between the number of out-of-hospital cardiac arrests and COVID-19.

- The first case of COVID-19 was confirmed in the Lombardy Region of Italy on Feb 20, 2020. Authors compared the number of out-of-hospital cardiac arrests during the 40 days after Feb 20, 2020, with the number from the same period in 2019. Among those with cardiac arrest in 2020, authors identified confirmed COVID-19 cases as well as those who had symptoms suggestive of COVID-19.

- During the study period in 2020, there were 9,806 reported cases of COVID-19. There were also 362 out-of-hospital cardiac arrests, a 58% increase from the 229 out-of-hospital cardiac arrests during the study period in 2019.

- The cumulative incidence of out-of-hospital cardiac arrests in 2020 was associated with the cumulative incidence of COVID-19 (Spearman rank correlation coefficient, 0.87; 95% CI 0.83, 0.91; P<0.001).

- 103 patients with out-of-hospital cardiac arrests were diagnosed with COVID-19 (16 patients) or had symptoms suggestive of COVID-19 (87 patients), accounting for 77% of the increase in out-of-hospital cardiac arrests.

- In 2020, compared with 2019, the median arrival time of the emergency medical service was three minutes longer. Among patients in whom resuscitation was attempted by trained personnel, the incidence of out-of-hospital death was 14.9% higher.

Aerodynamic analysis of SARS-CoV-2 in two Wuhan hospitals
Main message: Surface and air sampling within two hospitals and the community in Wuhan, China, demonstrated that SARS-CoV-2 genetic material was present in various concentrations in patient care, medical staff, and public areas. Factors that may reduce the concentration of viral genetic material in environmental samples include negative pressure isolation, ventilation of spaces, sanitization of surfaces (potentially including contaminated personal protective equipment), and crowd size reduction. The infectivity of detected virus was not assessed, and conclusions about infection risk could not be drawn.

- Authors conducted surface and air sampling (of total suspended particles and of size-segregated aerosols) in a low-acuity field hospital and a high-acuity hospital (which included negative pressure isolation facilities) designated for COVID-19 patients. Sampling was also conducted in select public areas such as pharmacies, residential buildings, and department stores. Authors quantified the amount of viral genetic material in samples; virus viability was not assessed.

- In the high-acuity hospital, minimal or no viral genetic material was found in air samples from patient care areas. In both hospitals, air samples from medical staff areas had higher concentrations of virus than samples from patient care areas. After implementation of rigorous sanitation procedures, the virus could no longer be detected in air samples from the medical staff areas of the low-acuity hospital. The highest concentration of virus was found in air samples collected in the un-ventilated toilet area of the low-acuity hospital.

- Surface contamination with viral genetic material was detected in contact-free patient care areas. Medical staff areas yielded the majority of contaminated super micron-range aerosols. Authors suggested that re-suspension of virus deposited onto surfaces, including personal protective equipment, may account for this finding.

- Low concentrations of virus were found in air samples from most public areas with the exception of a crowd-gathering area at a department store and a heavily trafficked area outside a hospital.
Characteristics and Clinical Outcomes of Adult Patients Hospitalized with COVID-19 – Georgia, March 2020

(MMWR, Early release 29 April 2020)

Main message: In examining a series of COVID-19 cases hospitalized in the state of Georgia, a disproportionate number of patients were black. Outcomes, including the proportion of black patients needing ICU care or mechanical ventilation, were similar to those of non-black patients. Black and non-black patients also had a similar proportion of deaths. Some patients in this study who died did not have underlying high-risk medical conditions recognized as putting them at risk for more serious illness.

- The study authors reviewed medical records of a sample of 305 COVID-19 patients hospitalized during March 2020 at eight Georgia hospitals in metropolitan Atlanta and southern Georgia. Among these patients, 62% were younger than 65 years old, 51% were female, and 83% were black.

- At four hospitals where most of the study patients were hospitalized, 80% of the COVID-19 patients were black, compared to 47% of hospitalized patients overall during the study period. Black patients were not more likely to need mechanical ventilation or to die compared to non-black patients.

- Older patients had longer hospital stays, were more likely to be admitted to the ICU, and more likely to die. Nevertheless, 23% of patients younger than 65 years and without a known high-risk comorbidity still required ICU admission and 5% died.

- Clear messaging about risk in all populations is necessary, as is specific messaging to at-risk groups based on local epidemiology.

Epidemiology and transmission of COVID-19 in 391 cases and 1286 of their close contacts in Shenzhen, China: a retrospective cohort study

(Lancet Infectious Disease, 27 April 2020)
Main message: Among a cohort of 391 index patients diagnosed with COVID-19, the infection spread to 6.6% of their close contacts overall, and to 11.2% of household contacts. These secondary attack rates were similar for children and adults. Surveillance and contact tracing may have reduced the time to diagnosis from onset of symptoms to diagnosis among the close contacts.

- Most of the index cases were identified through a system of symptom-based surveillance of people travelling to areas known to be affected by the outbreak (Hubei Province), and subsequently tested for SARS-CoV-2. Contacts were tested regardless of symptoms.
- All cases were treated at a designated hospital based on the level of care they needed. Asymptomatic contacts testing positive were isolated at centralized facilities. Persons identified through contact tracing who tested negative were quarantined either at home or a central facility and monitored for 14 days.
- At the time of identification, those identified through symptom-based surveillance had symptoms for an average of 4.6 days before being isolated. Contact tracing reduced the time from symptom onset to isolation to 2.7 days.
- Contact tracing was thought to reduce the transmission of disease based on secondary cases being effectively isolated. The mean $R_o$ for all index cases was 0.4, although 80% of secondary infections were caused by just 8.9% of cases.

COVID-19 Among Workers in Meat and Poultry Processing Facilities, 19 States, April 2020

(MMWR, 1 May 2020)

Main message: As in congregate living facilities, congregate work facilities such as meat and poultry processing plants pose special challenges for preventing and controlling transmission of COVID-19. Symptom screening of workers, policies encouraging ill workers to stay home, and physical distancing, as well as use of cloth masks and more frequent disinfection of high touch surfaces are recommended to decrease transmission.
The CDC was alerted to cases of COVID-19 among several meat and poultry processing facilities in early April 2020 and responded by performing on-site and remote assessments, in addition to broadly requesting more data from states to evaluate and analyze the situation.

Twenty-three states had reported at least one person in the industry affected by COVID-19, and 19 of these states provided aggregate data on a total of 4,913 patients meeting their case definitions. When the overall number of workers at the facilities was available, it was determined that 3% of workers in the industry were diagnosed with COVID-19 (range 0.6% – 18.2%). Twenty deaths were reported.

In addition to structural and operational challenges to effective infection prevention and control measures at these facilities, sociocultural and economic challenges were also noted. These included language barriers, employees traveling to and from work together, employees living together, and attendance bonuses that discouraged workers from staying home when ill.

Administrative and engineering controls as well as personal protective measures to minimize hazards to their workers need to be augmented during outbreaks to protect the health of the industry and its workers.

**Contact Tracing Assessment of COVID-19 Transmission Dynamics in Taiwan and Risk at Different Exposure Periods Before and After Symptom Onset**

(JAMA Internal Medicine 1 May 2020)

**Main message:** With high secondary transmission of COVID-19 prior to and immediately after symptom onset, mitigation measures such as contact tracing and isolation of symptomatic patients alone may not be enough to adequately control disease spread. More generalized community measures such as physical distancing should be employed. A better understanding of early transmission dynamics could identify the most effective control strategies to minimize disease transmission.

A series of 100 index cases with lab-confirmed COVID-19 and their 2,761 close contacts were identified and followed prospectively.
Among the index cases, the median age was 44 years (range 11-88 years), and 44% were women. Close contacts included household members, other family members not living in the same household, health care personnel, and others with 15 minutes of face-to-face contact without appropriate personal protective equipment.

- Close contacts were only tested if they developed symptoms consistent with COVID-19. The researchers identified 22 symptomatic cases among the 2,761 contacts, for an overall secondary clinical attack rate of 0.7% (95% CI 0.4% – 1.0%). The secondary attack rate was highest for household members and non-household family (4.6%, 95% CI 2.3% – 9.3% and 5.3%, 95% CI 2.1%-12.8% respectively).

- The secondary attack rate was also higher for those with presymptomatic exposure or exposure within five days of symptoms onset compared to those with exposure after five days of symptoms onset. Overall, the authors observed a decreasing secondary attack over time.

- None of the 91 close contacts who had exposure to an asymptomatic index case became clinically ill with COVID-19, and 4 of the 1097 close contacts with exposure to a mildly ill index case became ill. In contrast, 6 of the 275 close contacts who had exposure to a severely ill index case became clinically ill. The relative risk of secondary illness when exposed to severe cases appeared to be higher but did not reach statistical significance (RR 3.99, 95% CI 1.0 – 15.84).

**Cleansing and Disinfectant Chemical Exposures and Temporal Associations with COVID-19 – National Poison Data System, United States, January 1, 2020 – March 31, 2020**

(MMWR, 24 April 2020 – prior to news around ingesting disinfectants)
Main message: Compared to the same time period in 2018 and 2019, from January 1 – March 31, 2020, poison control centers across the United States received significantly more calls related to exposures to disinfectants and cleaners, with a sharp increase in the beginning of March, 2020, coinciding with the COVID-19 pandemic affecting the US and prior to media coverage regarding other potential roles for these products in pandemic response. To avoid chemical exposures, users should always follow manufacturers’ directions, and take steps such as using gloves and avoiding mixing of chemicals to minimize their risk. All potentially hazardous chemicals including household cleaners and disinfectants should be kept out of reach of children.

Clinical Features

Clinical value of immune-inflammatory parameters to assess severity of coronavirus disease 2019

(IJID 22, April 2020)

Main message: In this retrospective study, high levels of the immune-inflammatory markers interleukin-6 (IL-6) and C-reactive protein (CRP) independently correlated with severity of disease in 127 COVID-19 patients. In addition, in a multivariate logistic regression, hypertension was an independent risk factor for severe disease.

- The authors used clinical parameters to differentiate between mild, moderate and severe/critical disease, and grouped the patients into non-severe vs severe disease. There were 111 patients classified as non-severe, and 16 classified as severe. Patients in the severe group were older, had higher BMI, and were more likely to have hypertension.

- Patients in the severe group had higher baseline levels of CRP, IL-6, neutrophil-to-lymphocyte ratio, fibrinogen, sialic acid, interleukin-10, and interferon-γ (all p<0.05). There was no difference in other measured lab parameters, including lactate, pH, cardiac troponin-I, and pro-B natriuretic peptide.
- In a multivariate regression model, IL-6, CRP and hypertension were each independent risk factors for severity of disease. In addition, in an area-under-the-receiver-operating-characteristics model (AUROC) predicting risk of severe disease, including these three parameters had the highest predictability value.

- Decreasing levels of IL-6 also correlated with recovery of severity for 12 of the 16 patients with severe disease.