SARS-CoV-2 and COVID-19 Executive Daily Digest
The University of Kansas Executive Daily COVID-19 Digest Working Group
DATE: April 29, 2020

Daily Overview
- This working group will provide daily evidence updates to healthcare providers, hospitals leadership, policymakers and the public on issues related to the coronavirus pandemic.
- The Daily COVID-19 Digest includes information about:
  (A) Tracking and Anticipating Spread and Hospitalizations
  (B) Health Care Decisions
  (C) Pharmacologic Treatment of COVID-19
  (D) Relevant Government Actions
  (E) Other Relevant Developments

Pandemic Status (as of the end of April 28, 2020)

<table>
<thead>
<tr>
<th></th>
<th>Confirmed cases</th>
<th>Deaths</th>
</tr>
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<tbody>
<tr>
<td>The University of Kansas Health System*</td>
<td>314</td>
<td>12</td>
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<tr>
<td>Wyandotte county</td>
<td>585</td>
<td>53</td>
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<td>Global</td>
<td>3,130,191</td>
<td>217,674</td>
</tr>
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</table>

*TUKHS had a total of 121 hospital admissions. Data about death is from April 23
Key Highlights

- **New predictions include Kansas State, KC metro, Wichita and greater KS locations outside of KC and Wichita metro areas.** Rates of new COVID-19 cases in KS are affected by new cases identified in the KS regions outside of the KC/Wichita metro areas. It will be critical to follow these numbers closely and assess their effect on hospitalization and deaths over the next weeks.

- There are a multitude of different antibody tests for COVID-19 with variable performance. Tests vary in the viral antigen(s) they target. It is not yet clear which antibody responses, if any, are protective or sustained. A "positive" test is exceptionally difficult to interpret because the performance of these tests is not well known. For some assays both sensitivity and specificity may be poor, or at the very least undefined. Details in the digest [Link]

- Physical distancing and decreasing the number of contacts is working, and remains an essential element, to slow the spread of COVID-19 – ‘flatten the curve’. Stay home and stay safe!

- Assuming continued physical distancing at current levels, peak utilization is expected to occur between mid-April and end of May 2020. The total peak number of hospitalizations range between 250 total hospitalizations in Kansas (best case) to 422 (worst case) in the models that are most closely matching the data to-date.

- Based on the best available evidence to date, until a sufficient medical intervention is able to be deployed broadly, it remains likely over the longer term that COVID-19 will persist in our community to varying degrees that will require continued management.

- Additional data through significantly expanded testing, and hospital reporting, will be critical for continued management of COVID-19 over the foreseeable future, including to ensure the most informed decision making by State and local government officials, and community leaders. Here why:
  - Evidence-based models that predict the total number of infections, peak number of infections, timing of peak healthcare utilization and need for hospital beds/ICU beds/ventilators currently vary widely in their predictions because of incomplete understanding of the most important factors. These factors are: the rate of infectivity in particular geographic areas, with and without accounting for physical distancing efforts; the expected duration and timing of physical distancing; the rate of asymptomatic and/or mild illness in the population; and the rate of hospitalization, ICU and ventilator needs per case detected.

  - Similarly, to project local PPE requirements, data is needed on historical PPE use, projected PPE use per COVID-19 known/suspected patient, the total/peak number of infections, the severity of illness (home care vs. hospitalized vs. critical care) and the likely distribution of COVID-19 patients throughout KS

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A. Tracking and Anticipating Spread and Hospitalizations

**Projected local spread**

As of April 27th, 2020 the available data on confirmed cases, hospitalizations, ICU use and deaths could be consistent with different predictive models. The updated predictions based on a variety of widely used models for COVID-19 pandemics suggest that:

- We are likely to experience a prolonged but **fluctuating plateau.** We remain uncertain about the "shape of the curve". We are likely to have a slower and more prolonged downward trend and could experience other “peaks” in the future.

- Data driven predictions are very close to actual observed numbers of deaths

- Data driven predictions are higher than actual observed numbers of cases- likely because of low testing except in the KS regions outside of the KC/Wichita metro areas (i.e Southwest Kansas) where
reported cases are exceeding predictions. This may relate to the identification of few clusters in these areas.

- It will be critical to follow closely the number of new cases in different metro areas and assess their effect on hospitalization and deaths over the next weeks.
- There is more uncertainty about hospitalization data because of different assumptions (e.g. proportion of cases hospitalized, length of stay...etc). However, no matter what model we use, it is very unlikely that we will reach healthcare capacity in the next 4 weeks at the state level. However, metro areas with small hospitals and limited inpatients and intensive care capacity may reach capacity rapidly.
- Having accurate data about cases, hospitalizations, and deaths is essential to ensure we can identify early any concerning signs of another “peak”.

We will continue to update the models according to actual data and continue to test the models assumptions daily.
Parabolic models are estimated with a constant, linear and quadratic terms for number of days since the initial case was reported in each state (beginning January 25, 2020). This functional form allows for the possibility that the increase in the number of cases could decrease, i.e. that mitigation efforts could ‘flatten the curve’ (in contrast to continued exponential growth). This framework allows for the calculation of the maximum number of new cases (e.g. where the curve reaches a maximum and begins to decline.

Estimates from the IHME (Institute for Health Metrics and Evaluation) at the University of Washington are derived from the implied death rate using reported CDC statistics. The revised IHME model was updated multiple times, with the latest update on April 27, 2020 after revising estimates based on additional available data and assumptions. Estimates were revised to better fit observed data including adjustments to account for international data, to allow for different effects of social distancing across locations, and to better fit areas with a small number of confirmed cases. Importantly, the revised IHME model assumes physical distancing using the New Zealand Government alert system Level 4 which is consistent with existing, robust physical distancing in effect in Kansas as of April 1st, and this model assumes that these physical distancing measures will stay in place until the end of May.

CHIME model estimates generated at https://penn-chime.phl.io/. Inputs for population (KS, 2,814,700; KC, 2,501,151; Wichita, 675,126), market share (100%), date of first reported case (3/7/20 for KS and KC, 3/13/20 for Wichita), and previous number of hospitalizations (KS, 263; KC, 200; Wichita, 30). Default values were used for all other parameters. Population for KC and Wichita includes counties in the Combined Statistical Area (CSA) as defined by the US Census Bureau. The CHIME model, as depicted, was run as of April 1st, and assumes a constant rate of additional COVID-19 hospitalizations based on trends on that date. The mitigation effects of government mandated physical distancing on COVID-19 hospitalizations were not fully apparent as of April 1st. This model has been revised to account for changes in hospital treatment variables, such as hospital length of stay. Unlike the revised IHME model, however, it has not been revised to account for the additional effects of physical distancing that have been realized.

The numbers of new cases and hospitalizations in other areas in the state are small and insufficient to make accurate forecasting predictions.
The effect of physical distancing on the number of contacts and the extent of the infection

The basic rate of infection spread depends on (a) the period of infectiousness (approx. 14 days); (b) the number of close contacts a person has, and (c) the likelihood of transmission of the virus to a susceptible person with each contact. The primary goal of physical distancing is to reduce the effective rate of infection by reducing the number of contacts each person has. There is incomplete understanding of how physical distancing efforts have influenced the number of close contacts the average individual has. Agent-based transmission models simulate daily interactions between people and can project the fraction of the population that will become infected under various social-distancing scenarios (figure below; for example, the blue trace demonstrates active infections under the assumption of 6 contacts per person per day before physical distancing and 2 contacts per person per day after social distancing). Making different assumptions substantially alters the projections for the total fraction of the population eventually affected (<5% vs. >15%). The impact of physical distancing dramatically affects the number of individuals needing hospitalizations and/or intensive care (including mechanical ventilation). The model with 3 daily contacts suggests about 1,000 hospitalizations in KS at peak versus 14,000 hospitalizations with 4 daily contacts. Reduction in the number of contacts is the goal of physical distancing. Every effort must be made to maximize adherence by citizens to participate in the ‘stay at home’ orders and minimize physical contact with others to whom they could unintentionally transmit the virus.

B. Health care decisions

Personal protective equipment (PPE) for health care personal and patients in the hospital

PPE for healthcare personnel is needed to protect both individual providers and the healthcare system itself. Inadequate PPE supply may result in shortage of healthcare personnel due to infection and/or quarantine. Infected healthcare personnel may also act as a vector for transmission to patients. Hospitals and healthcare systems, including TUKHS, face challenges in projecting PPE requirements and availability. Projections of future health system PPE use follow projections for total number of persons under investigation (PUIs) or contracts hospitalized, and ICU patients, emphasizing the urgency of reliable projections. Additional information about spread of COVID-19 disease and different PPE can be found in appendix 1.
**Information needed to make informed projections about the required PPE during the pandemic**

- Reports of number of patients hospitalized, admitted to the ICU and requiring mechanical ventilation (available from data about hospitalized patients)
- Estimates of forecast of number of patients hospitalized, admitted to the ICU and requiring mechanical ventilation with best- and worst-estimate of when the peak will occur (best and worst-case scenarios) (remains a ‘work in progress’)
- Historic utilization of PPE per isolated patient (available from data about hospitalized patients)
- PPE required per COVID-19 positive/suspected patient (available from data about hospitalized patients)
- Historical hospital market share, and projections of whether this is expected to remain stable throughout the course of COVID-19 surge (remains a ‘work in progress’)
- Expected number and severity of cases in a specific hospital (both total and per week)
- Period of time that social distancing/community mitigation strategies must remain in place to manage the outbreak (remains a ‘work in progress’)

**C. Pharmacologic Treatment of COVID-19**

- On April 24, 2020, the FDA issues a warning for use of hydroxychloroquine or chloroquine for COVID-19 outside of the hospital setting or a clinical trial due to risk of heart rhythm problems.
- On April 3, 2020, the FDA approved plans for nationwide trials of the convalescent plasma and hyperimmune globulin.
- On March 28, 2020, the FDA approved plans for nationwide trials of the convalescent plasma and hyperimmune globulin.
- On March 27, 2020, the FDA approved compassionate use of convalescent plasma for serious or immediately life-threatening COVID-19 infections under a single patient emergency Investigational New Drug authorization.
- Regimens under investigation (excluding vaccine candidates): Sarilumab (antibody against IL-6R-alpha), Tocilizumab (more potent antibody against IL-6), Nitric Oxide gas inhalation, Remdesivir, Chloroquine or Hydroxychloroquine, monoclonal antibodies from convalescent serum, Lopinavir-Ritonavir combination, Lopinavir-Ritona combination + interferon-beta.
- Clinical Trials: >90 clinical trials worldwide of various regimen from the list above.
- **SOLIDARITY trial:** (Remdesivir; Lopinavir/Ritonavir; Lopinavir/Ritonavir with Interferon beta-1a; and chloroquine or Hydroxychloroquine) Large global 4-arm randomized clinical trial launched by the WHO on 3/20/2020 with a sample size of 10,000 hospitalized patients. The U.S. is not yet participating in SOLIDARITY.
- DISCOVERY: French add-on study to SOLIDARITY with 3200 participants in France, with a similar design and drug regimen as SOLIDARITY.
- U.S. Clinical Trials: a large number of actively recruiting clinical trials using sarilumab, nitric oxide gas inhalation, remdesivir, hydroxychloroquine, monoclonal antibodies from convalescent serum or lopinavir-ritonavir combination.
- The University of Kansas Medical Center is participating in the Healthcare Worker Exposure Response and Outcomes of Hydroxychloroquine (HERO HCQ) trial, a nationwide clinical trial to evaluate the effectiveness of hydroxychloroquine (HCQ) in preventing COVID-19 infection in exposed health care workers. The trial launched April 22. It is a phase-3 double-blinded clinical trial, funded by the Patient-Centered Outcomes Research Institute (PCORI). It is accompanied by a registry, launched April 14, that will create a community of health care workers who have expressed interest in contributing to the scientific community's understanding of the impact of COVID-19. [https://heroesresearch.org/hero-hcq/?fbclid=IwAR2FlYbiDffmXezuqEeu9CGQe-F_KxUS1xkEoQRRMk6pQ6zjiNYObDe5bo](https://heroesresearch.org/hero-hcq/?fbclid=IwAR2FlYbiDffmXezuqEeu9CGQe-F_KxUS1xkEoQRRMk6pQ6zjiNYObDe5bo)
A registry of clinical trials can be found on the WHO (link) and clinicaltrials.gov (link) websites.

D. Relevant legislative actions
As part of ongoing efforts to limit the spread of COVID-19:
- On April 15, 2020, Governor Laura Kelly extended the statewide stay-home order until May 3rd 2020.
- On March 29, 2020, the president extended the nationwide social distancing guidelines for another 30 days, to end on April 30th 2020.
- On March 28, 2020, Governor Laura Kelly issued Executive Order to institute a temporary, statewide stay-home order for 21 days, to end on April 19th 2020.
- Updates available here.

E. Other Relevant Developments
Testing (Antibody testing)
- Expanding testing and more sustained strategies for widespread testing and surveillance are going to be essential to follow up the true impact of this pandemic.
- On April 1, 2020, the Food and Drug Administration (FDA) issued an Emergency Use Authorization (EUA) for a qualitative test for the detection of IgM and IgG antibodies against SARS-CoV-2. https://www.fda.gov/media/136622/download (accessed April 5, 2020). When evaluating the available data, serologic testing appears promising to advance the knowledge about diagnosis and immunology of COVID-19. However, it may not be ready for wide use among the public yet.
  - There are a multitude of different antibody tests for COVID-19 with variable performance. Tests vary in the viral antigen(s) they target. It is not yet clear which antibody responses, if any, are protective or sustained.
  - The antibody response in infected patients remains largely unknown, and the clinical values of antibody testing have not been fully demonstrated.
  - A "positive" test is exceptionally difficult to interpret because the performance of these tests is not well known. For some assays both sensitivity and specificity may be poor, or at the very least undefined.
  - Some FDA-authorized COVID-19 antibody tests are estimated to have 96-98% specificity, which would mean that a positive test result is more likely to be a false-positive result than a true positive result in low prevalence area like KS.
- Both Wyandotte and Johnson Counties expanded community-based testing programs that will greatly increase the number of tests performed on community members. This will likely increase the numbers of new cases diagnosed. It should be noted, however, that this should not increase the number of hospitalizations unless there is an increase in the number of cases beyond the increase in testing.

Social impact
- Early data suggests racial/ethnic and socioeconomic disparities affecting the case detection and fatality rates of patients with COVID-19.
- On April 3, 2020, The Center for Disease Control (CDC) recommended wearing cloth face coverings in public settings where other social distancing measures are difficult to maintain (e.g., grocery stores and pharmacies), especially in areas of significant community-based transmission. This
recommendation is meant to address the high rates of asymptomatic patients in the community who may be able to spread the virus. Wearing a face mask in a community setting does not protect the wearer from acquiring infection. Understanding of the transmission risk associated with wearing a face mask remains incomplete; however, COVID-19 is thought to spread mainly through close contact from person-to-person in respiratory droplets from someone who is infected.

**Update**
This is a living document. Information in this document will need to be revised and updated in the near future. We will conduct ongoing reviews of the available evidence and continuously monitor the data to determine if information require modification. Based on the rapidly evolving nature of this pandemic, information will likely need to be updated daily. This document is not intended to establish clinical practice guidelines or the standard of care. Physicians should exercise their own clinical judgement in the care of individual patients.
Appendix 1
SARS-CoV-2 is spread via respiratory droplets from talking, coughing, sneezing, and close contact with symptomatic individuals. Procedures like surgery, endoscopy or bronchoscopy can also lead to aerosolization and subsequent airborne transmission. Human-to-human transmission can occur from unknown infected persons (e.g. asymptomatic carriers or individuals with mild symptoms) as well as individuals with virus shedding during the pre-incubation period before symptoms develop. Data related to the spread of SARS-CoV-2 in the early phase of the pandemic have confirmed that healthcare personnel are at higher risk of infection than the general population. Several types of PPE are available and summarized below. The WHO has issued guidance on the use of PPE, following a three-pronged strategy: (1) minimize the need for PPE, (2) ensure PPE use is rational and appropriate, and (3) coordinate PPE supply chain management mechanisms. WHO has developed recommendations for PPE use. KUHS Infection Prevention has developed similar, parallel, recommendations.

<table>
<thead>
<tr>
<th>Types of PPE</th>
<th>PPE</th>
<th>Use</th>
<th>Pros and Cons</th>
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</table>
| Surgical or medical   | Surgical or medical masks | - Droplet precautions- block large particles (>5 μm) | - Widely available  
- Does not require fit testing  
- Cannot be re-used |
| N95 mask respirator   | N95 mask respirator | - Filter at least 95% of aerosols (<5 μm) and droplet-size (>5μm) particles | - Requires fit testing  
- Can be used for an extended period and re-sterilized |
| powered air-purifying  | powered air-purifying Respirator (PAPRs) | - Provide high level protection from common airborne viruses that exceed N95 face masks | - Does not require fit testing  
- Provides head and neck protection  
- Can be re-used by the same healthcare provider |
| Gloves                | Gloves       |                                                                      | - Does not require fit testing  
- cannot be reused |
| Gowns                 | Gowns        |                                                                      | - Does not require fit testing |

5This KU COVID-19 Executive Digest is authored and updated by Reem A. Mustafa and Tami Gurley-Calvez (lead authors), Daniel Parente, Mark Meyer, Robert Moser, David Wild, Jack Beal, Edward Ellerbeck, Ian Thompson, Laura Mussulman, Caitlin Smith, Christian Dodge, Akinlolu Ojo and Joseph LeMaster.
References


