COVID-19 Portfolio for L.K. Tuominen, Ph.D.

1. "COVID-19 Update: Projecting Mortality Rates." 28 April 2020. Powerpoint slide set sent to the offices of Ohio State Senator Sandra Williams and Ohio's 11th Federal District Representative Marcia Fudge.

   This slide set documents my thought processes related to the use of public data provided by the Ohio Department of Health as I developed the minimum mortality model. Estimates for minimum mortality across the seven-state COVID-19 cooperation region, and within each of the seven states, were based on data from Marion and Pickaway Counties in Ohio. The specific estimates for each of the seven states in the region were provided to Ohio Senators Sherrod Brown and Rob Portman in hard copy, I believe in the same package as Portfolio Item #2. On July 10, 2020, I provided an update to the offices of State Senator Williams and Congresswoman Fudge with corrections and new maximum mortality estimates, which I have applied at the county (OH), state, seven-state region, and national levels. Based on these efforts, my current estimate for COVID-19 deaths across the U.S., Washington, D.C., and all territories is 211,000-552,000 individuals.

2. 8 May 2020. Template of letter sent in hard copy to the offices of Ohio Senators Sherrod Brown and Rob Portman.

   This letter documents formal scientific outreach to my Senators, an effort that drew on multiple scientific thinking skills to advance evidence-based solutions to help mitigate a national emergency. The letter provides specific recommendations related to potential treatments for COVID-19, interpretation of genomic information published in the news media, and possible avenues to improve COVID-19 testing efficiency and reliability. As of July 10, 2020, I do not intend to reach out to the Ohio Senators on issues related to COVID-19, unless maximum mortality thresholds reported to Congresswoman Fudge's office are exceeded.

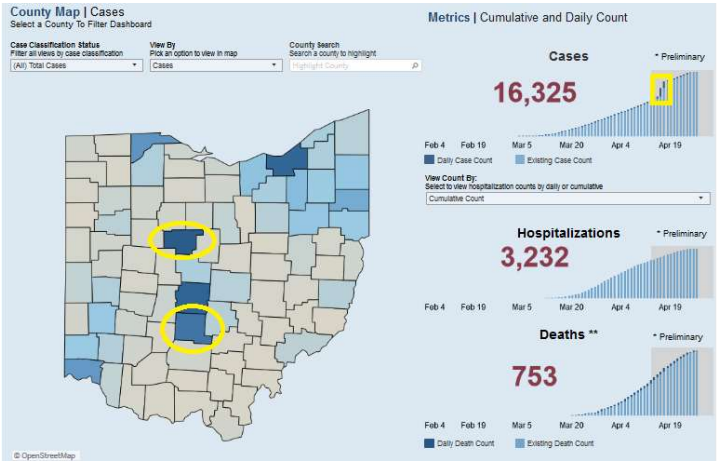
3. "COVID-19 Data Reporting for 6/11/20." 11 June 2020. E-mail sent to the office of Ohio's 11th Federal District Representative Marcia Fudge.

   This e-mail documents the fifth in a series of weekly reports monitoring five- or seven-day average case counts across the seven-state region. Data transparency and reliability is assessed for each state. To support efficient allocation of limited resources, some county-level information is provided for Ohio and, because mortality was over 80% of the projected minimum determined in late April, for Michigan. During weeks six and seven, a brief analysis of racial disparities was provided for Ohio. Each week, the same information is also sent to the Ohio Green Party, Ohio Department of Health, State Senator Sandra Williams, Congresswoman Marcia Fudge, and Senators Brown and Portman. The final report in this series was sent on July 2, 2020. I am currently working to identify partners to delegate and scale up this approach to crisis resource allocation.

COVID-19 Update: Projecting Mortality Rates

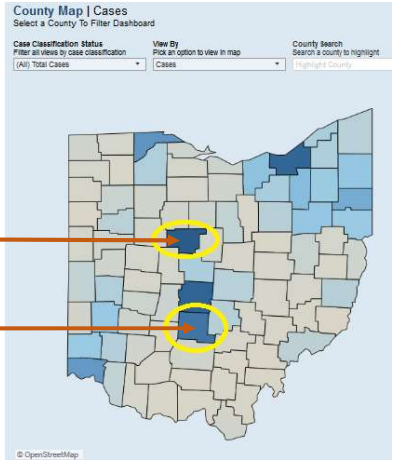
L.K. Tuominen, PhD
John Carroll University
April 28, 2020

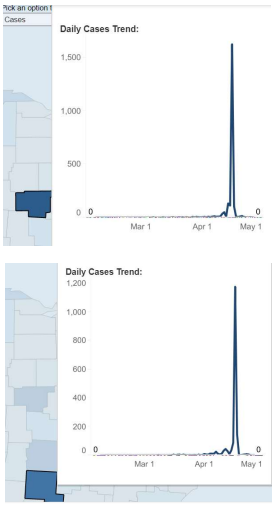
Where We Stood on Monday



"Spikes" from Random Sampling

Inferred random testing in Marion and Pickaway Counties





Marion County
2188 Positive Tests

High Signal to Noise Ratios

Pickaway County
1698 Positive Tests

Where Are We on the Curve?

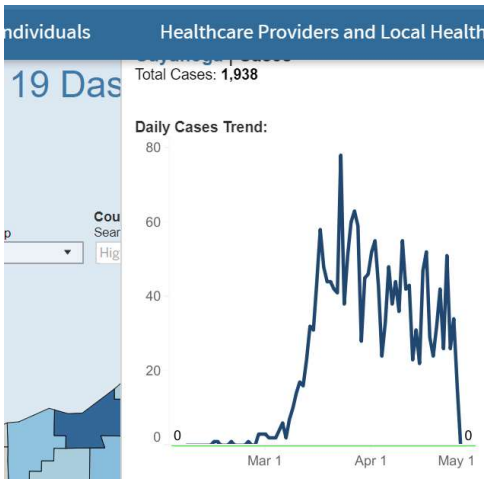
Random testing results make case count data difficult to interpret

Convex curve shape?

Inflection Point?

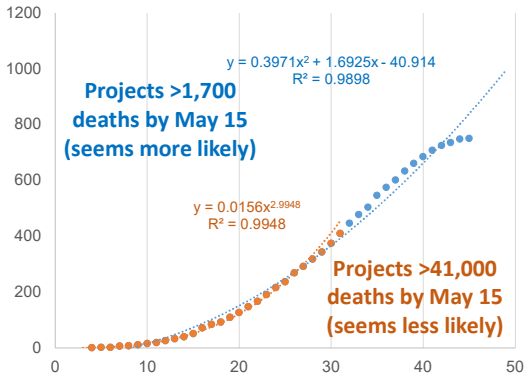
How is Cuyahoga County Doing?

- Cuyahoga County was "ground zero" in Ohio
- State reporting as of Monday:
  - 1938 cases
  - 522 hospitalizations
  - 96 deaths
- Daily case counts suggest that Cuyahoga County is beyond the inflection point
  - Social distancing is working
  - Case counts could still increase with return to "business as usual"

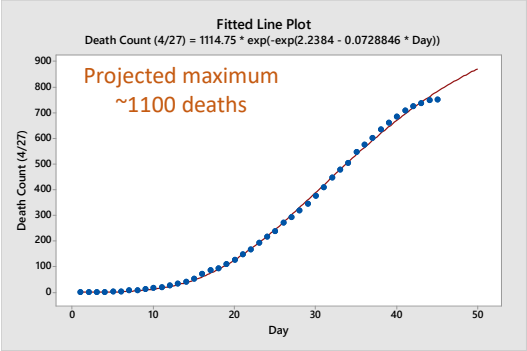


Model Assumptions Matter

Power Law Model vs. Quadratic Model

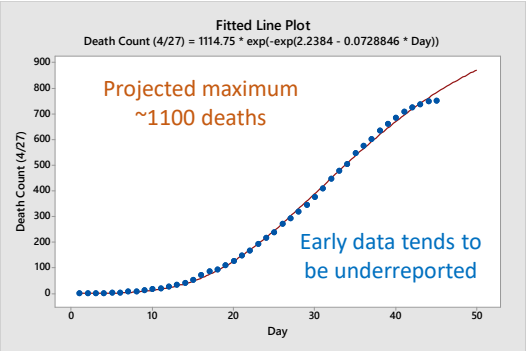


Sigmoid, Without Data Censoring

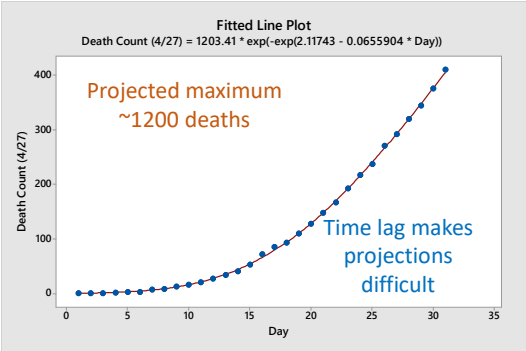


Model Assumptions Matter

Sigmoid, Without Data Censoring

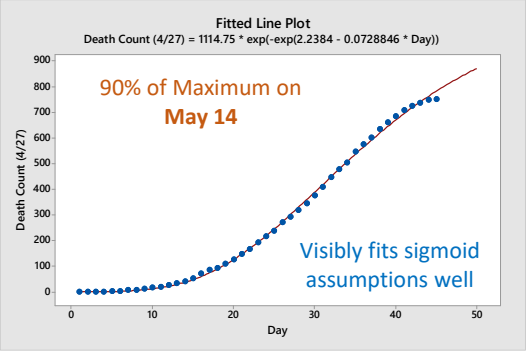


Sigmoid, With Data Censoring

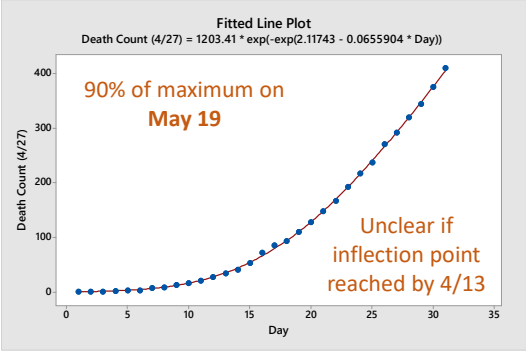


Model Assumptions Matter

Sigmoid, Without Data Censoring



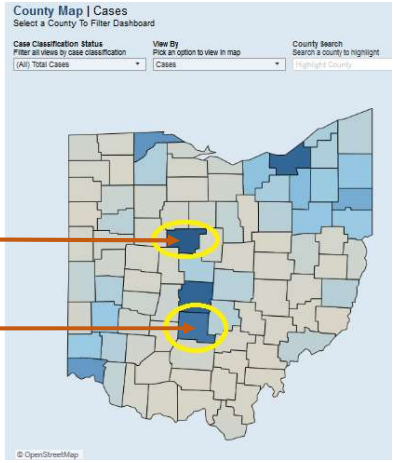
Sigmoid, With Data Censoring

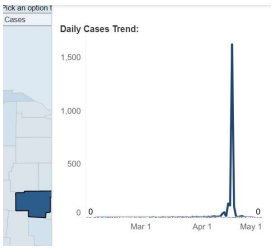


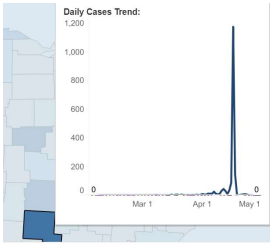
Reasonable for Policymakers Averse to Public Health Risks to Delay Reopening Beyond May 1

Projections from "Spike" Data

Random testing in Marion and Pickaway Counties







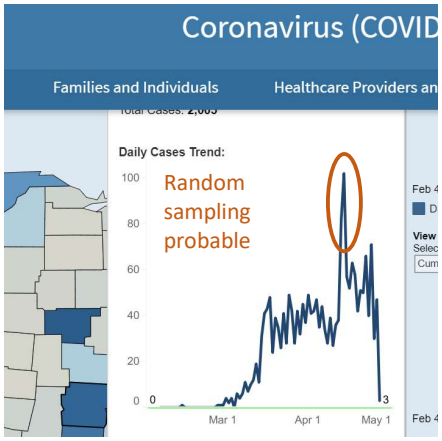
Marion County
2188 Positive Tests

Strongest Signal to Noise Ratios

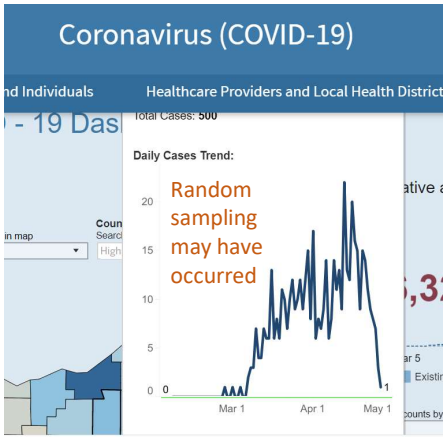
Pickaway County
1698 Positive Tests

More Signal to Noise Examples

Franklin County



Summit County



Making "Spike" Data Projections

Rapid Response Method

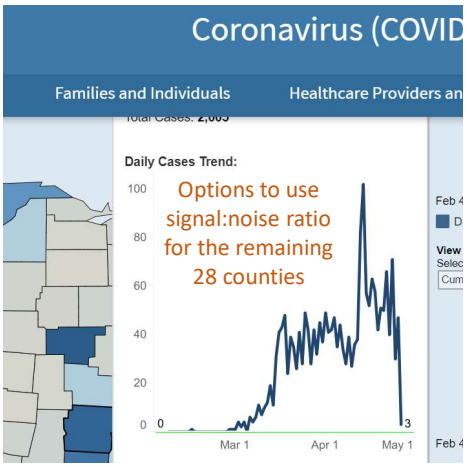
- Gather county population data
- Calculate "minimum true positive" rate for Marion & Pickaway
- Extrapolate minimum positives and minimum projected deaths

"Back of the Envelope" Projections

- State of Ohio
  - Minimum 330,000 positive as of 4/17
  - Minimum 7,400 deaths projected
- Seven state COVID-19 alliance
  - Minimum 1.6 million positive cases
  - Minimum 36,000 deaths

Why More Information is Needed

- Both methods assume spatial homogeneity
- New method assumes entire county was sampled
  - If 10,000 individuals sampled in each county, true minimums are ~5x higher
- New method is best applied when few case numbers reported
  - Left portion of the curve
  - Relevant in 60 OH counties
- The q-RT-PCR test for the virus also has a high error rate
  - Inherent uncertainty in the data requires upper bounds as well



Final Summary

- Ohio Department of Health is demonstrating good practices for COVID-19 data gathering and transparency
- Modeling similar to that used in previous reports to Governor DeWine during March/April 2020 suggests a "responsible restart" would not occur before **May 14th**
- Simple method using Ohio Department of Health random sampling data suggests the state will see a **minimum** of 7,400 COVID-19 deaths
- Maximums could be 5-fold higher or more – **analysis is ongoing**

My profuse thanks to all of those in Ohio working to contain COVID-19!

8 May 2020

Dear Senator:

Thank you for your service to the people of Ohio during the COVID-19 pandemic crisis. I am writing today to discuss the molecular biology of the SARS-CoV-2 virus, rather than statistical projections of incidence and mortality. Generating accurate statistical projections now depends on ensuring that the tests we are conducting have good accuracy. Accuracy depends in part on the underlying biology.

I understand that some have questioned whether SARS-CoV-2 has been genetically engineered. Briefly, I concur with expert assessment that this is not the case, given the available genomic information reported by the *New York Times* on April 3, 2020.[1] I have not conducted a full independent analysis, but that is potentially within reach at a future date, given my prior training in genomics.

Nonetheless, the widely-disseminated information on the viral genome highlights some relevant policy considerations that may be of interest to the health of the people of the United States. My focus in this briefing is a close reading of information surrounding NSP12, which the authors of the *New York Times* article called the "copy machine" that "assembles genetic letters into new virus genomes." This was intended as lay language to indicate the enzyme *RNA-dependent RNA polymerase*, which uses an RNA template to produce a sequence of RNA that is complementary to (i.e., can form a double helix with) the original. The genetic sequence of NSP12 is of interest for multiple reasons.

First, the *New York Times* reports that NSP12 is a target for remdesivir, which has previously been established as an inhibitor of other RNA-dependent RNA polymerases.

- Dr. Fauci reported last week that a Phase I clinical trial supports the use of remdesivir in reducing the duration of COVID-19 symptoms. Thus, both the available phenomenonlogical (human-scale) and mechanistic (molecular) understanding of remdesivir at this time suggest treating COVID-19 with remdesivir is medically valid.
- To the best of my knowledge, these two criteria have not yet been met for hydroxychloroquine sulfate or chloroquine phosphate, which have previously been used in treating malaria, rheumatoid arthritis, and lupus.
- Given the available information, **I believe sufficient evidence is now available to support expansion of production of remdesivir, but not that of hydroxychloroquine sulfate or chloroquine phosphate, under the Defense Production Act.**
- Given the global prevalence of malaria, any excess production of the latter two medications that has occurred in the U.S. during 2020 can certainly be allocated to that use.

The authors state that "the infected cell begins reading the RNA sequence for NSP12," then repeats the "reading" of one nucleotide, "c" (cytosine) once before proceeding.

- Here, the authors are describing how human cells invaded by the SARS-CoV-2 virus engage in translation of the viral RNA to produce the NSP12 protein. Translation requires molecular "machinery" comprised of a standard "toolkit" of other RNA and proteins.
- To the best of my knowledge, translation does not typically involve any intentional "backtracking" of the sort described. Thus, the authors' choice was interesting in the sense that they may have been attempting to draw biologists' attention to the sequence and function of NSP12.
- Another possible explanation is that the three-dimensional structure of NSP12 does somehow disrupt the enzymatic machinery of the host cell to cause re-reading of a single nucleotide. This explanation seems less likely to me, but I have not assessed its validity.

The authors state that another protein, NSP11, is encoded in the same region as NSP12.

- Based on my analysis of the NSP12 genetic information, any such protein is a maximum of 68 amino acids in length.
- I am not aware of any functional enzymes that are less than 100 amino acids in length. However, human insulin is comprised of two proteins, one of which is 21 amino acids in length and the other, 30 amino acids in length. Insulin acts as a hormone, or signaling molecule, in the human body.
- The authors state that it is unclear whether or not the "tiny protein" NSP11 has any function. Based on the lengths of candidate sequences that may represent NSP11, it is fair to speculate that this protein could potentially have some function related to cellular or physiological signaling in the body.

Again, I would like to emphasize that I am working exclusively from genomic information presented in the *New York Times* article. A more appropriate analysis of NSP11 would link full genomic data with chemical data from protein samples of the virus.

Finally, I would like to revise my concerns about testing for SARS-CoV-19 presented over the phone yesterday. **I believe the RT-PCR test should only be applied to individuals who are presenting symptoms consistent with COVID-19, after a minimum of two, and preferably three, additional layers of testing.** A more appropriate testing protocol is provided in Appendix 1. The first two tests are relatively trivial and would require the Senate (or preferably, Congress as a whole) to provide thermometers & pulse oximeters to all employees, enabling self-monitoring and reporting in outcomes for the duration of the pandemic. **Expanding the third layer of testing nationwide according to the proposed test protocol would require expansion of CT scanner production under the Defense Production Act.** The chest CT scanner method has previously been demonstrated to be more reliable than RT-PCR testing for COVID-19.[2] Anecdotally, the U.S. health care system has lagged behind the rest of the world in its use of this

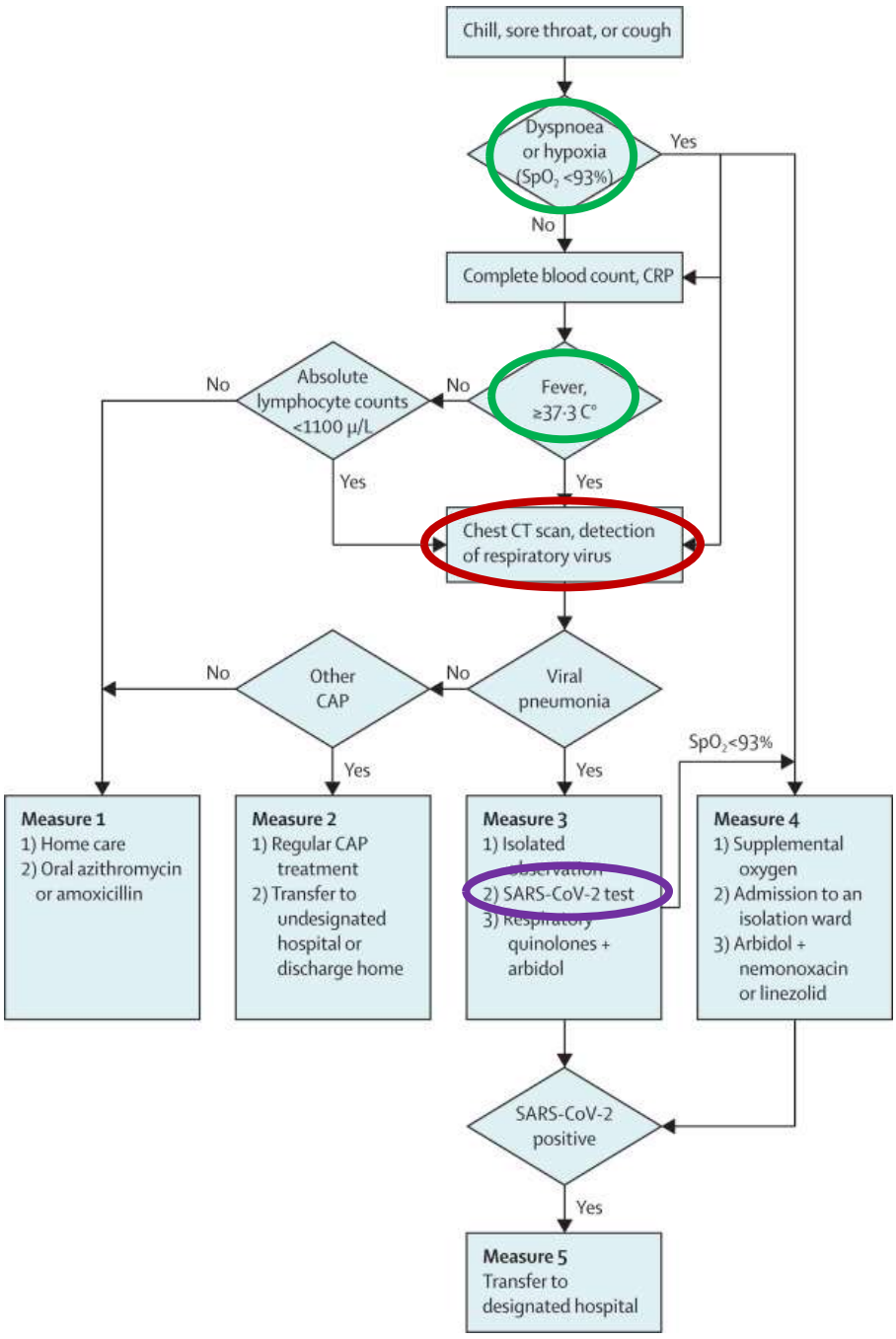
technology even prior to the pandemic, so enhanced production would have benefits beyond the pandemic. Finally, recent research suggests that RT-PCR testing for SARS-CoV-2 is most appropriately applied to sputum samples rather than other types of biological samples.[3] Changing this portion of the RT-PCR test itself has the potential to improve the reliability of SARS-CoV-2 test results throughout the nation. This, in turn, would improve model projections for incidence and morbidity. To the best of my knowledge, the only cost of such a change is that of disseminating the correct information.

Thank you for hearing my concerns,

L.K. Tuominen, Ph.D.

Encl. (2)

Appendix 1: Appropriate COVID-19 Testing Protocol



Flow chart provided to a group of 190 e-mail addresses by Mary Odum of Gainesville, FL. Circled items represent key tests for COVID-19. Green represents potential measures at employer level. Red represents key bottleneck in U.S. health care system. Purple represents measure carried out within health care system that requires a procedural change implemented nationwide for improved data reliability.

Appendix 2: References

[1]Corum, J. and Zimmer, C. 3 April 2020. "Bad News Wrapped in Protein: Inside the Coronavirus Genome." *New York Times*. https://www.nytimes.com/interactive/2020/04/03/science/coronavirus-genome-bad-news-wrapped-in-protein.html

[2]Ai, T., et al. 26 February 2020. Correlation of Chest CT and RT-PCR Testing in Coronavirus Disease 2019 (COVID-19) in China: A Report of 1014 Cases. *Radiology* (In Press) https://pubs.rsna.org/doi/pdf/10.1148/radiol.2020200642

[3]Yu, F., et al. 28 March 2020. Quantitative Detection and Viral Load Analysis of SARS-CoV-2 in Infected Patients. *Clinical Infectious Diseases* ciaa345 https://doi.org/10.1093/cid/ciaa345

COVID-19 Data Reporting for 6/11/20

L.K. Tuominen <lktuominen@hotmail.com>

Thu 6/11/2020 10:38 AM

To: Clifton.Williams@mail.house.gov <Clifton.Williams@mail.house.gov>

Dear Mr. Williams,

Thank you for your service to Ohio's 11th District in the office of Congresswoman Marcia Fudge!

I am reporting in with the fifth weekly status update for regional COVID-19 case count averages and associated recommendations. As before, data are reported as five-day averages for the previous four weeks, using data from Sun-Thu, with a one-week embargo. This week, I am also providing new county-level information for Ohio, which I hope will be helpful to Congresswoman Fudge.

My temperature this morning was 98.2 F.

Illinois:
Week of 5/10: 2370 new cases/d
Week of 5/17: 2046 new cases/d
Week of 5/24: 1607 new cases/d
Week of 5/31: 1168 new cases/d
Summary: Five day average new case counts declined during the previous two weeks.
Action: Illinois may REMAIN OPEN. Recommend to close again if/when the average case count data exceeds 2370 new cases/d.

Indiana:
Week of 5/10: 510 new cases/d
Week of 5/17: 523 new cases/d
Week of 5/24: 428 new cases/d
Week of 5/31: 426 new cases/d
Data Reporting Note: A net change of -126 positive cases was present in the Indiana data set during the period of April 19-May 25 relative to the values reported last week. It is unclear on what basis COVID-19 case numbers would be removed from the database.
Summary: Five day average new case counts declined during the previous two weeks. Indiana has one orange flag for three weeks of unexpected losses in previously reported case numbers.
Action: Indiana may REMAIN OPEN. Recommend to close again if/when the average case count data exceeds 639 new cases/d.

Kentucky:
Week of 5/10: n/a
Week of 5/17: 126 new cases/d
Week of 5/24: 176 new cases/d
Week of 5/31: 218 new cases/d
Data Reporting Note: Due to the lack of fully transparent data reporting, I will record Kentucky case counts and mortality reported by the state on Tuesdays. I will use two data points to calculate 7-day averages.
Summary: Average daily case counts increased during the past two weeks. Kentucky continues to have two red flags for poor data transparency for time-course data on case counts and mortality counts.
Action: Under CDC guidelines, Kentucky should REMAIN CLOSED. I strongly recommend making reopening contingent on achieving a level of data transparency that enables rapid independent assessment of case counts and mortality over time.

Michigan:
Week of 5/10: 716 new cases/d [+10 relative to previous report]
Week of 5/17: 376 new cases/d [+6 relative to previous report]
Week of 5/24: 215 new cases/d [+25 relative to previous report]
Week of 5/31: 160 new cases/d
Data Reporting Note: Michigan has updated its data reporting practices for both case count and mortality time-course data, ensuring improved data transparency.
Summary: Average case counts declined during the previous two weeks.
Action: Michigan has met CDC guidelines and MAY REOPEN. Recommend to close if/when average case count data exceeds 376 new cases/d.
Addendum: Michigan has exceeded 88% of the projected minimum mortality I calculated for that state in late April. Approximately 77% of Michigan's COVID-19 deaths have occurred in three areas: **Wayne County (including Detroit), Oakland County, and Macomb County**. I STRONGLY RECOMMEND DIRECTING ANY SURPLUS HEALTH CARE RESOURCES WITHIN THE SEVEN-STATE REGION TO THESE THREE COUNTIES.

Minnesota:
Week of 5/10: 646 new cases/d [+9 relative to previous report]
Week of 5/17: 771 new cases/d [+3 relative to previous report]
Week of 5/24: 547 new cases/d [+42 relative to previous report]

Week of 5/31: 403 new cases/d
Data Reporting Note: The State of Minnesota reports that data for the most recent 7 day period are preliminary.
Summary: Average case counts have decreased during the past two weeks, with the difference between averages for the weeks of 5/24 and 5/31 is greater than the change in the average for the week of 5/24 relative to the previous report.
Action: Under CDC guidelines, Minnesota MAY REOPEN. Recommend to close if/when average case count data exceeds 646 new cases/d.

Ohio:
Week of 5/10: 540 new cases/d [+14 relative to last week's report]
Week of 5/17: 546 new cases/d [+25 relative to last week's report]
Week of 5/24: 403 new cases/d [+60 relative to last week's report]
Week fo 5/31: 303 new cases/d
Data Reporting Note: Public data for 5/26 through present are considered preliminary by the State of Ohio.
Summary: Average case counts decreased during the past two weeks. The difference between averages for the weeks of 5/17 and 5/24 is greater than the change in the average for the week of 5/17 relative to last week's report. This is also true for the weeks of 5/24 and 5/31.
Action: Under CDC guidelines, Ohio may REMAIN OPEN. Recommend to close again if the average case count data for the week of 5/31 exceeds 526 new cases/d. This recommendation is more conservative than those for other states due to the longer time period required for data reporting.
Addendum: COVID-19 mortality reported for **Monroe County, Mahoning County, and Pickaway County** has exceeded projected minimums I calculated in early May (previously unreported). In addition, mortality reported in **Lucas County and Columbiana County** has exceeded 84% and 97%, respectively, of their respective projected minimums. I RECOMMEND DIRECTING SURPLUS HEALTH CARE RESOURCES WITHIN OHIO TO THESE THREE COUNTIES.
Local Reporting: New 5 day case count averages increased in **Cuyahoga County** from the week of 4/19 through the week of 5/17 (maximum 82 new cases/d), then decreased during the weeks of 5/24 (62 new cases/d, preliminary) and 5/31 (51 new cases/d, preliminary). Due to Ohio's data reporting practices, it is too soon for me to evaluate whether these change are large enough to represent a decreasing trend.

Wisconsin:
Week of 5/10: 267 new cases/d
Week of 5/17: 340 new cases/d
Week of 5/24: 419 new cases/d
Week of 5/31: 332 new cases/d
Summary: Average case counts declined from the week of 5/10 to the week of 5/17, increased from the week of 5/17 to the week of 5/24, and decreased from the week of 5/24 to thew week of 5/31.
Action: Under CDC guidelines, Wisconsin should REMAIN CLOSED for at least one additional week.

With the numerous large peaceful protests during the past two weeks, we should remain cognizant of the possibility of rapid increases in COVID-19 cases later this month. Although I have not previously examined racial data for COVID-19, I recently learned of this resource which can be helpful in understanding the racial disparities in the impacts of the pandemic: https://covidtracking.com/race

Best wishes,
L.K. Tuominen, Ph.D.