Summary of Initial Modeling Efforts – COVID-19 in Iowa
Whitepaper Prepared for the Iowa Department of Public Health
by the University of Iowa College of Public Health COVID-19 Response Group

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The COVID-19 modeling team at the University of Iowa has taken a multi-disciplinary, multi-model approach to estimating the progression of the COVID-19 outbreak in the State of Iowa. Rather than be limited by a single modeling approach, utilizing different models can allow us to ask different nuanced questions, which will give us a more comprehensive understanding of the outbreak and allow for more effective forecasting of the impact of interventions on the outbreak. We are concurrently developing and evaluating three modeling paradigms which can each be used to accomplish separate but complementary goals. The three different approaches and their goals are as follows.

> (M1) A short-term prediction model with few modeling assumptions designed to make accurate one-week ahead forecasts. This model additionally serves to evaluate the plausibility of longer-term predictions based on the current short-term trajectory of the COVID-19 outbreak.

> (M2) A medium-term prediction model providing the potential range of the outbreak, yielding estimates of disease characteristics and important prediction bounds for the ongoing outbreak in Iowa. The disease characteristics included in the model are latent and infectious periods of COVID-19 as well as mortality rate.

> (M3) A model designed to evaluate various policy changes related to nonpharmaceutical interventions such as increasing or relaxing social distancing measures or implementing universal face shields. This model will be able to provide projections of how we expect the disease to spread if social distancing measures are implemented at various points in time.

Taken together, these approaches should allow the team to understand the current and immediate state of the COVID-19 outbreak in Iowa, quantify the size and scope of the outbreak in the coming months, and characterize how various actions may affect the trajectory of the outbreak. All results presented here are based on publicly available state-level data using models developed by the team. The team has not yet had sufficient time to develop extensions using the supplied IDPH data.

Conclusions: We have found evidence of a slowdown in infection and mortality rates due to social distancing policies, but not that a peak has been reached. The current data does not support a conclusion that the reproductive number has been brought below 1. There is considerable uncertainty still in how many cases and deaths Iowa could eventually have, with possible projections between 150 and >10,000 total deaths. Therefore, prevention measures should remain in place. Without such measures being continued, a second wave of infections is likely.

Model 1: Short term forecasts and trajectory assessments

Overview. This model projects the longer-term outbreak epidemiology (e.g., out to 6 months) by estimating the most-likely outbreak trajectory in the short-term (e.g., 3-14 days) and comparing trajectories over the near-term period. This approach uses only location-specific data (e.g., from Iowa) to estimate the short-term trajectory. Thus, it aims to avoid possible misspecification or conforming to the trajectories observed in other states or locations that have characteristics or social distancing policies different from Iowa. Note that the validity of short-term forecasts is continuously evaluated by comparing forecasting performance against a similar model applied to different locations or time periods; this allows the model to avoid "over-fitting" the limited amount of information that is currently available in Iowa. Model fitting is also performed dynamically so that changes in an outbreak may be detected and more quickly integrated into the projections.

The methodological approach can be described in three parts.

- First, a relatively simple short-term model is built to forecast the outbreak trajectory over the next 3-14 days, depending on the optimal state-specific lag between input and outcome measures. In the example below, the short-term model leverages the relationship between the lagged number of positive cases and the cumulative mortality rate. (Note: this approach can be extended to other outcomes.)
- Second, "feasibility bounds" around these short-term projections are constructed by evaluating "out-of-sample" performance, which is derived by comparing many different prior short-term forecasts to the observed values in different locations and time periods.
- Third, long-term trajectories are estimated by evaluating those that best conform to out-of-sample performance. For example, a long-term trajectory may be deemed "too extreme" if it represents a deviation from the short-term forecast that exceeds 95% of all out-of-sample estimates. This third step can be done using external long-term models (e.g., IHME model) or by fitting various models through the plausible points contained in the short-term feasibility bounds described in step 2.

Preliminary Findings. We have evaluated this model in two ways. First, we compared this approach to updated projections of the IHME model since it was unveiled on March 25th. This short-term fitting approach does a good job of anticipating revisions in the IHME projections, by

identifying state forecasts that appear to be over or underestimating the short-term trajectory in the coming days. Second, we applied this model to the most recent counts in the state of Iowa and constructed various long-term trajectories through different feasibility bounds, using the basic "curve-fitting" approach in the IHME model. Figure 1 depicts short-term forecast feasibility bounds for cumulative mortality in the coming week based on out-of-sample performance using the previous two weeks of forecast estimates in the states of IA, MN, WI, NE, SD, MO and IL. The feasibility bounds correspond to 50%, 80% and 90% of the out-of-sample prediction errors (e.g., 50% of the out-of-sample forecasts errors would suggest a true value within the 50% percent feasibility bound.)

Figure 1: Short-term forecast out-of-sample feasibility bounds
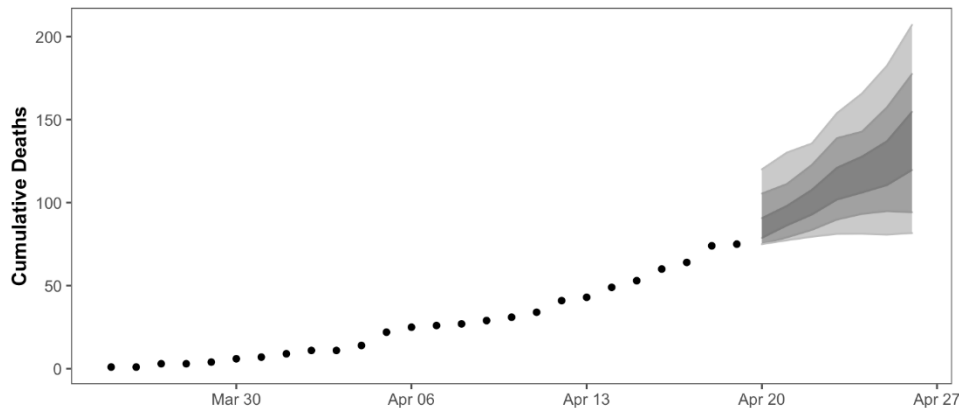Feasibility bounds for 50%, 80% and 90% of predictions

Figure 2, below, depicts five possible trajectories using the short-term forecast bounds depicted above for the next 7 days. These trajectories represent plausible trajectories within the 95% prediction interval (based on out-of-sample performance) that are also consistent with the most recently observed data. This figure also depicts the corresponding peak dates (for peak daily mortality) and total mortality by July 1st that corresponds to these points.

Figure 2: Plausible long-term trajectories
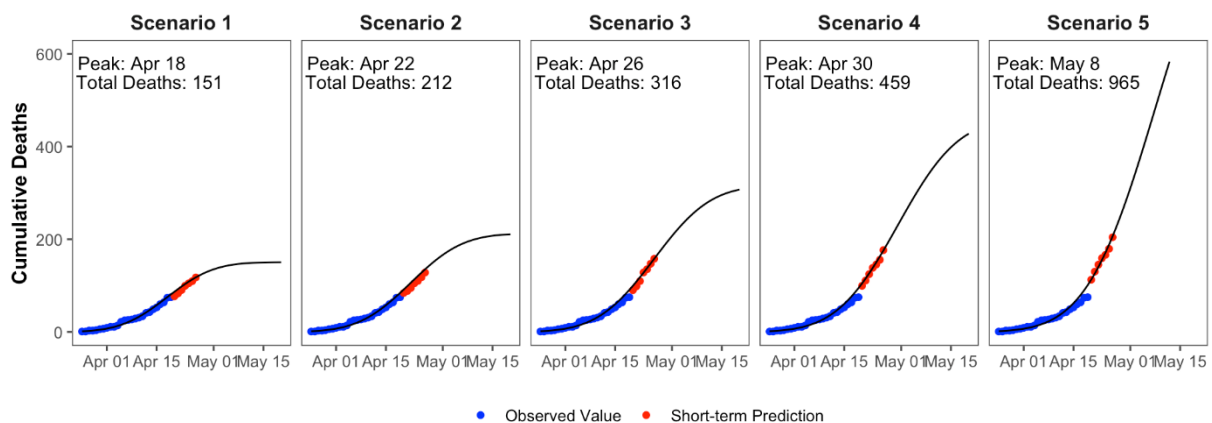
These figures demonstrate that a wide range of plausible trajectories still exist for the state of Iowa, ranging from 151 deaths (peaking on April 18th) to 965 deaths (peaking on May 8th). However, given the continued increased in positive cases, hospitalizations, ICU admissions and patients on ventilators, it is our opinion that Scenarios 1 and 2 are far less likely. Note that

Scenarios 1 and 2 represent peak mortality occurring this past Saturday or this coming Wednesday; these represent peaks occurring earlier than most existing forecast estimates for the state of Iowa. **However, it is important to note that the long-term trajectories plotted in Figure 2 assume the parametric shape and underlying social distancing assumptions of the IHME model, and this short-term model fitting approach should <u>only be used to assess the short-term plausibility</u> of a given trajectory and not to generate long-term forecasts.**

Model 2: Long term forecasts and disease characteristics

Overview. M2 takes a population-level approach to the spread of COVID-19 in Iowa, focusing on the reported mortality as a reliable, though lagged indicator of epidemic spread. This model is designed to synthesize available information about the latent and infectious periods of the COVID-19 infection, as well as existing public health interventions in the United States and abroad. With these tools, we evaluate the preliminary projections available by considering Iowa-only mortality, and also describe a range of plausible future projections assuming that the patterns observed elsewhere are applicable to the situation in Iowa.

Uncertainty remains about the mortality rate of COVID-19, and the best information indicates that it is heterogeneous by age, among other factors. Nevertheless, reported COVID-19 mortality may provide a useful perspective on the epidemic more broadly. This model posits that the true mortality rate is around 2%, but allows the estimate to be updated based on available data. This prior mean is consistent with Lai et. al. (2020), but may be conservative (Baud et. Al., 2020). M2 is a stochastic SEIR model, tracking population counts in the Susceptible, Exposed, Infectious, and Removed disease states. The latent period, during which individuals in the Exposed (E) category are infected but not yet actively transmitting the pathogen, was assumed to last between 2 and 14 days (95% probability), with typical values around 5 days (Lauer et. al., 2020). Much less is known about the infectious (I) period, which was assumed to last between 10 and 32 days (95% probability), with typical values around 14 days, based reports about recovery times.

Preliminary Findings. Regions affected by COVID-19 vary widely with respect to both the baseline transmission intensity, as well as the degree/type of community and policy response to the epidemic. We therefore consider two approaches to understanding the current situation and expected trajectory in the state of Iowa. First, we consider models of the trajectory of mortality in Iowa under varying assumptions and compare these trajectory results to comparable fits in other states and countries further along in the outbreak. This comparison gives rise to the results presented in Figure 3, in which we see substantial variability in the Basic Reproductive Number (R_0) by location. We estimate R_0 for each location using the Empirically Adjusted R_0 (EA-RN) calculated prior to the start of public health interventions. The EA-RN captures the expected number of secondary infections caused by each infectious individual in a specific context, sharing many of the same features as the commonly cited "Effective Reproductive Number".
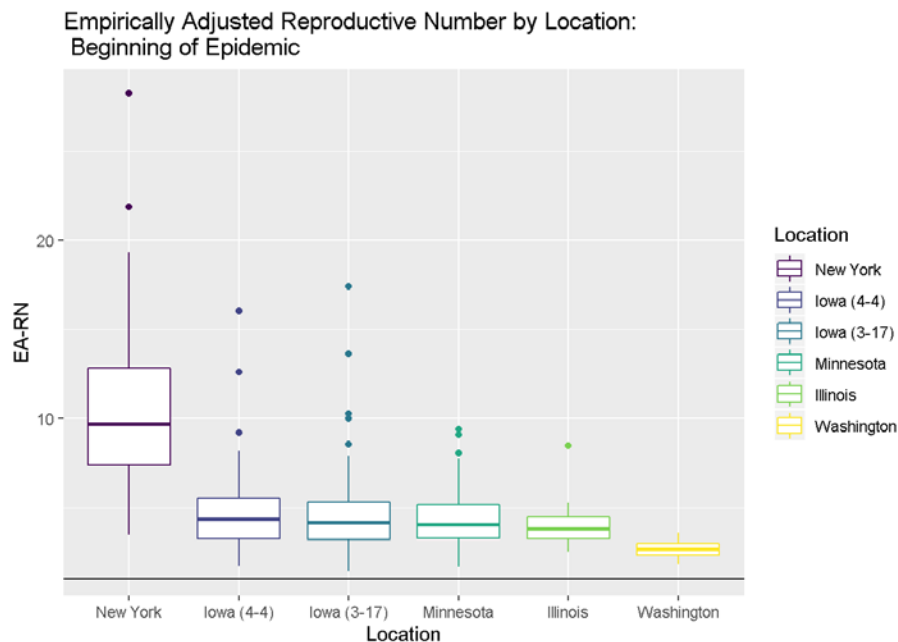
Figure 3. Estimated Empirically Adjusted Reproductive Numbers in selected regions, comparing the unmitigated epidemic intensity. Iowa is included here twice, once with interventions starting on 3/17/2020, and again with interventions assumed to begin on 4/4/2020. As expected, choices of intervention start time did not affect the estimated baseline (pre-intervention) epidemic intensity.

Building models purely on reported Iowa mortality data, we find that predictions are highly sensitive to assumptions about when contact behavior (social distancing) became widespread in the state, especially for longer term forecasts. In Figure 4, we illustrate the mortality curve of a model assuming that contact behavior began to shift on March 17th, when a Public Health Disaster Emergency was declared in the state. Here, we present the quantiles of fitted/projected cumulative mortality curves to show the range of likely/possible futures under this assumption. By May 28th, this model predicts a median mortality of 747 with a 95% interval between 156 and 9,734, reflecting a huge degree of uncertainty in trajectory and magnitude. This uncertainty is further shown by considering the model in Figure 5, where we modify the assumed date of behavior change to April 4th, at which point formal measures to close educational institutions were taken, and individuals and businesses had benefitted from more time to respond to changing circumstances. Despite being fit to the same data, this shift in the date on which contact behavior was allowed to change produced dramatic modifications to the six-week mortality prediction. The model estimated a median cumulative mortality of 1,369 on May 28th, with a 95% interval between 315 and 28,599. These projections will become more precise as more fatalities are observed, and hypothetical epidemics with incompatible shapes are discarded. In Figure 6, we present the Empirically Adjusted Reproductive Number curve for the March 17th intervention model. This measure is designed to capture the number of secondary infections per infectious individual observed in a particular population, and is related to the common "effective reproductive number", more flexibly capturing the change over time. As illustrated in the figure, we do not see strong evidence that the reproductive number has been brought below one. These initial results communicate several important points:

1. We see preliminary evidence for the impact of current imposed and adopted social distancing and contact mitigation efforts in Iowa, with cumulative mortality increasing more slowly than would be expected without such mitigations, and the reproductive number dropping over time.

2. We observe a huge range of possible outcomes, from relatively low fatalities to catastrophic loss of life. These models assume that the current measures taken to limit contact in Iowa remain in place, so while we see evidence that the epidemic intensity has decreased from the initial period of uncontrolled spread, there is not sufficient evidence in this data set alone to conclude that current measures will necessarily be sufficient to prevent a return to higher rates of transmission and corresponding mortality.
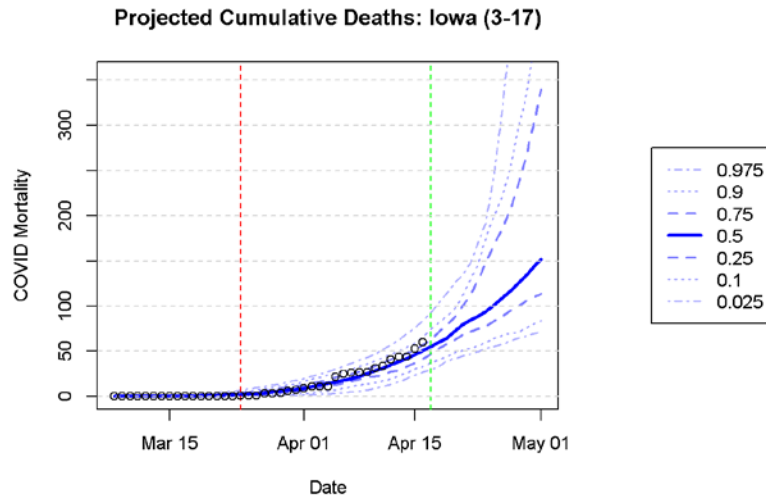
Projected Cumulative Deaths: Iowa (3-17)

Figure 4: Projected cumulative 2-week mortality in Iowa using only Iowa specific data, and assuming that a shift in contact behavior occurred on March 17th.
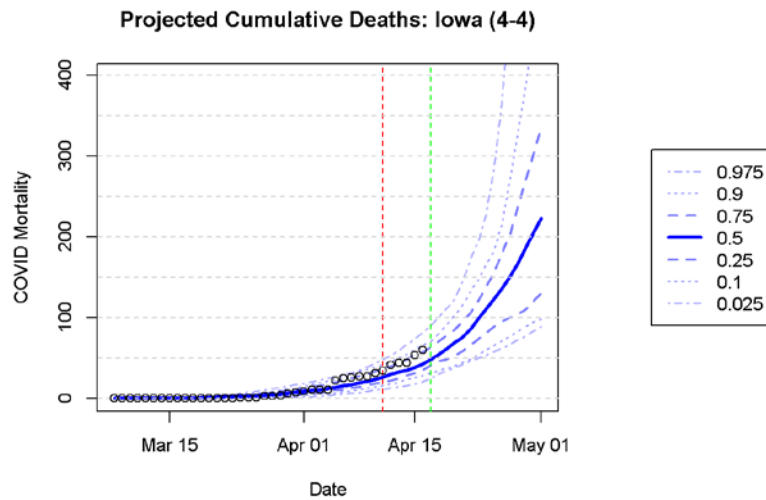
Projected Cumulative Deaths: Iowa (4-4)

Figure 5: Projected cumulative 2-week mortality in Iowa using only Iowa specific data, and assuming that a shift in contact occurred on April 4th.
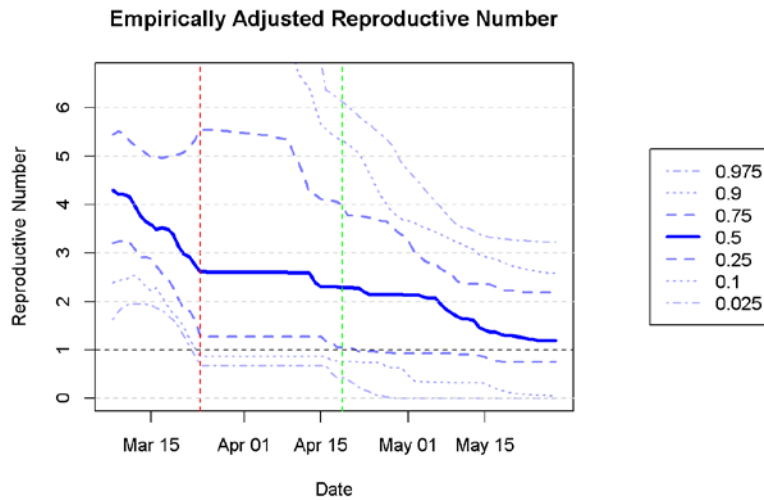
Empirically Adjusted Reproductive Number

Figure 6: Estimated Empirically Adjusted Reproductive Number curve, based on the March 17th Iowa only intervention model. Only when this value drops below one do we expect the epidemic growth to be sub-exponential. While it's clear that the reproductive number has dropped over time, we do not have evidence that it has fallen below one, or that it is expected to unambiguously do so in the immediate future.

In order to improve the precision of our forecasts, we can introduce assumptions about how the intervention in Iowa relates to that implemented in other locations. This approach allows us to borrow information about how the spread of COVID-19 has been fought in other places, without requiring that we assume the entire disease course in Iowa will be similar. Nevertheless, every state and nation can reasonably be expected to show different transmission dynamics, and the formal and informal responses to COVID-19 have certainly been highly varied in type, timing, implementation, and adoption. Thus, this approach is better suited for describing a range (from optimistic to pessimistic) of possible futures than for adopting a specific best prediction, unless strong evidence is presented to justify the substantial similarity between the responses of the locations under study. Table 1 presents this range of scenarios, varying by which state is used to inform prior knowledge of intervention efficacy, and which date is deemed most comparable to the intervention in that state. Figures range from extremely optimistic to moderate, and are compared to the results from the Iowa-only models given above.

Table 1: Expected Mortality Scenarios by 5/28 (NOT Total Mortality)			
Intervention Magnitude	**Intervention Estimated From:**	**Iowa Intervention Beginning On:**	**Median Mortality by 5-28 (95% Cr-I)**
Extremely Optimistic	New York	3/17/2020	107 (67-296)
Extremely Optimistic	New York	4/4/2020	334 (169-632)
Optimistic	Washington	3/17/2020	341 (133-1955)
Optimistic	Washington	4/4/2020	492 (240-1997)
Moderate	Minnesota	3/17/2020	560 (115-6219)
Moderate	Minnesota	4/4/2020	871 (200-10008)
Iowa Only	Iowa	3/17/2020	747 (156-9734)
Iowa Only	Iowa	4/4/2020	1369 (315-28599)

Overall, the results of M2 support evidence of "curve flattening", but **do not** definitively indicate that this will be quickly followed by the containment of virus spread. **While improved and ongoing mitigation is indicated as a plausible outcome, M2 also identifies risks of returning to a mode of increasingly rapid spread.** These results indicate that great caution is needed at this early stage before loosening of potentially insufficient containment measures is considered.

Next Steps. M2 is a population-level model, and as such it misses important heterogeneity in state populations. Extensions of this work should apply more granular data to better understand the distribution of COVID-19 cases in Iowa. In addition, in the next few weeks as more information about the mortality curve in Iowa becomes available, estimates for the peak time and final size of the epidemic based on M2 are expected to become more accurate, and the length at which forecasts will be meaningfully precise will increase. M2 is also able to accommodate a hypothetical relaxing of interventions, if expressed in relative terms (e.g., statements like "reducing intervention intensity to 85% of current levels"), or to similarly infer the likely effect of such policies if adopted first elsewhere.

Model 3: Evaluating polices

Overview. M3 is designed to describe disease transmission dynamics over a large contact network corresponding to the 3.155M residents of Iowa. By explicitly modeling how individuals contact one another, contact based interventions or the relaxing thereof can be tested virtually to understand how we might expect such interventions to affect the disease trajectory. While this model may be used to construct long-term predictions, its primary function is to understand how the disease curve can be manipulated by public policy decisions.

This model leverages information collected in prior studies (Kwok et al., 2018; Zhaoyang et al., 2018) to accurately reflect the human-to-human contact patterns. It computes the expected number of infectious individuals at any given date due to disease transmission through these contacts. The effects of increasing or decreasing social distancing can be implemented directly in a time-varying and individual-specific manner. Additionally, time-varying infective-susceptible transmission probabilities can be modeled explicitly, thereby allowing the estimation of the effect of, e.g., universal face shields on the disease curve.

Preliminary findings. An early utilization of M3 can shed light on several critical areas. First, we show that barring additional interventions such as contact tracing, we expect that reopening society to its pre-COVID-19 status anytime in the next four months will lead to a second wave of infections that will necessitate reimplementing our current social distancing policies. These estimates were based on an adaptive strategy of reopening society if the number of daily cases (both reported and unreported) fell below a threshold of 150, 100, 50, or 10, and reinstating our current level of social distancing if we observed 7 contiguous days of increasing number of daily cases. Figure 7 shows these results by plotting the expected number of daily cases according to the various thresholds. In all cases, a second peak emerges necessitating the reinstatement of social distancing policies.
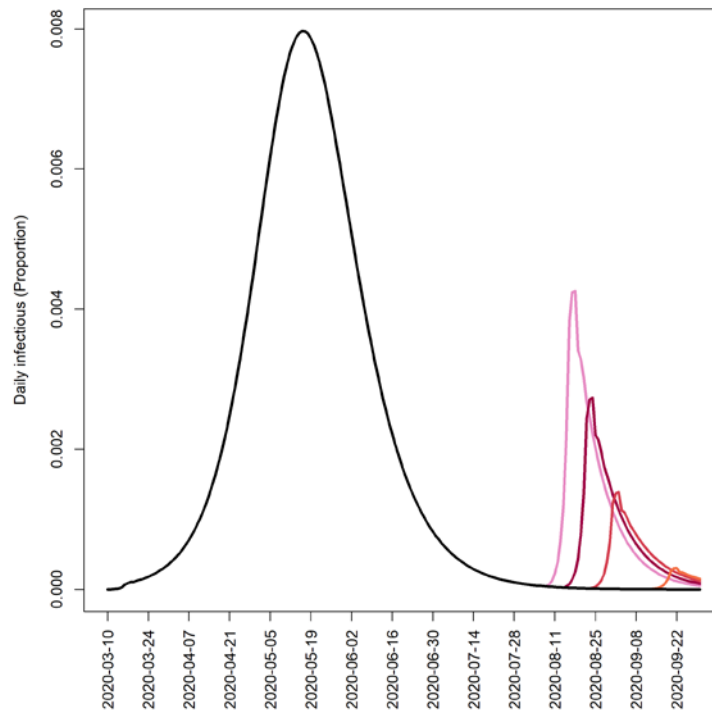
Figure 7. Expected number of daily COVID-19 cases over time with an adaptive strategy for reopening society. Social distancing will be relaxed if the number of daily cases drops below 150 (pink), 100 (purple), 50 (red), or 10 (orange) cases, and reinstated if 7 consecutive days of increasing daily case counts occurs. The black curve provides a baseline which maintains the current level of social distancing indefinitely.

We have also used M3 to evaluate the efficacy of universal PPE, such as face shields. To illustrate this approach, we evaluated universal PPE in terms of reduction in the probability that an infective-susceptible contact would lead to a transmission event. Figure 8 shows these results using the adaptive scheme described above with a threshold of 100 daily cases to reopen, where the universal PPE has been implemented starting on May 1, 2020. From this figure we see that even with low efficacy, the current peak drops considerably more rapidly than our current trajectory. However, reopening society is still highly likely to lead to a second peak unless the PPE efficacy is strong (at least 80% reduction in transmission probability).
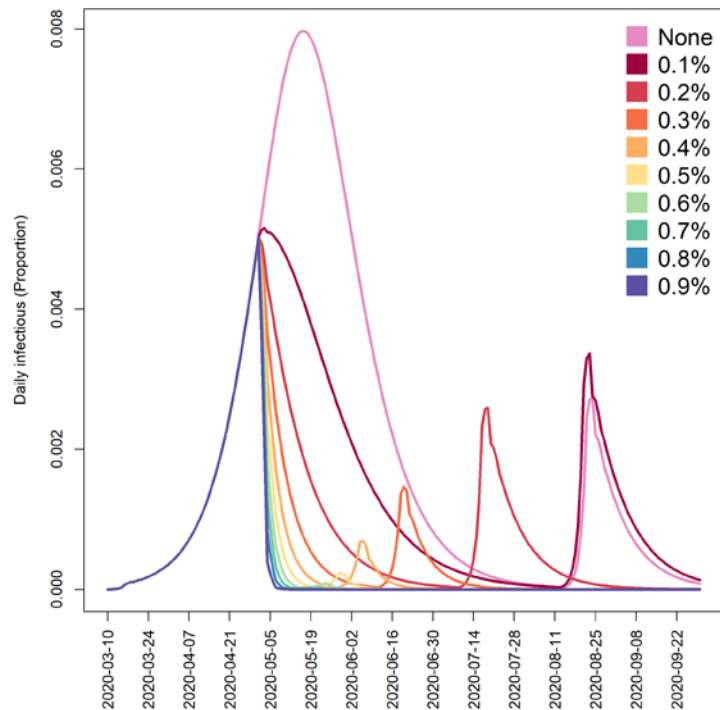
Figure 8. Expected number of daily cases due to varying levels of efficacy for universal PPE implemented on May 1st as an illustration. Efficacy is measured in terms of reduction in the probability of a susceptible-infective contact leading to a new transmission. The adaptive strategy for reopening and reimplementing shows that only with high efficacy rates does a second peak (and subsequent reinstatement of social distancing) fail to emerge.

Finally, we used M3 to evaluate the effect of opening society for all but those individuals with the highest contact rates. Figure 9 shows how reopening society based on contact rates works conjointly with PPE effectiveness. This figure shows that if we can maintain the current quarantining levels for those with the 20% highest contact rates through, e.g., limiting large social events, we can greatly diminish the impact of the second wave, and a lower level of PPE efficacy is required to eliminate the second wave entirely (50% reduction in transmission probability).
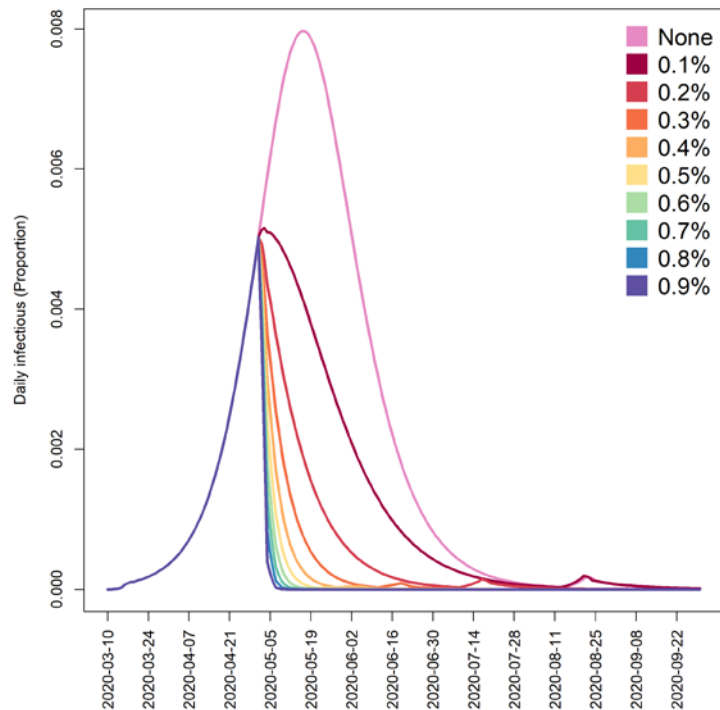
Figure 9. Expected number of daily cases due to varying levels of efficacy for universal PPE implemented on May 1st as an illustration. Efficacy is measured in terms of reduction in the probability of a susceptible-infective contact leading to a new transmission. The adaptive strategy used here maintains quarantining at the current level for those with the highest number of contacts while reopening society for the rest. Pairing this with medium efficacy universal PPE, a second peak (and subsequent reinstatement of social distancing) may not emerge.

Future directions. The current model is limited in that the model is being trained on the true number of cases which can only be estimated. The preliminary results presented here are based on publicly available data alongside current estimates of unreported cases in the United States (Jagodnik et al., 2020). The data received by IDPH this past week will allow us to better estimate the true number of cases, thereby increasing the accuracy of our assessments and forecasts.

In addition, we are developing a web-based tool for IDPH and other interested parties to use in order to evaluate specific changes in social distancing practices and universal PPE use. We will notify IDPH as this tool becomes available for use.

References

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