

# COVID-19 Mathematical Modeling: Preliminary Results & Next Steps

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May 28, 2020

## Executive Summary:

- Initial modeling results suggest that a combination of contact tracing, asymptomatic surveillance (testing each person once every 14 days) and a low initial prevalence (supported through testing students upon returning to campus) would result in fewer than 1% of the campus population requiring hospitalization under a nominal set of parameters, assuming a full return of students, faculty and staff in the fall semester. This can be reduced further with more frequent asymptomatic testing and stronger efforts to screen those returning to campus. If enacted, this would dovetail with a complementary effort at Cornell to reduce transmissions through housing policy, class organization, and regulations on social gatherings.
- At the same time, modifying modeling parameters by only a modest amount from these nominal values results in greater risk of morbidity and mortality. Some parameter combinations, that we consider to be not implausible, can yield serious consequences if interventions do not adjust to meet the challenge. Such outcomes point to the need to design a robust early-warning system. Regular asymptomatic testing as evaluated here can supply the signal needed to detect such outcomes.
- Moreover, such scenarios suggest that the best course of action may be one that can *adapt* to facts on the ground, e.g., by adjusting asymptomatic screening frequency based on observed prevalence, or by beginning with stronger protections for vulnerable populations that can be relaxed if the risk level permits.
- Under a range of plausible parameter setting, regular asymptomatic testing is essential to keeping the epidemic under control; without it we see a significant risk for high hospitalization rates. We envision that this asymptomatic testing would be enabled by the capacity at Cornell's Animal Health Diagnostic Center, with costs controlled through group testing. Work continues with collaborators in the College of Veterinary Medicine to validate group testing protocols and obtain regulatory approval.
- Toward the goal of quantifying uncertainty, we are continuing efforts to estimate parameters, provide ranges of plausible parameter values against which we should plan, and investigate the impact of modeling assumptions. We are becoming more confident in the predictions as

laid out in this document as we learn more about model input parameters, but estimates may also change as we gain more information and add more modeling fidelity.

- In parallel, we are using the model to investigate quarantine capacity requirements, the impact of having vulnerable individuals stay away from campus, and modifications to student housing.
- This is a work in progress and continued input is welcomed from Cornell’s Health Considerations Committee, Cornell’s Teaching Reactivation Committee, and others.

## 1 An Overview of Methods and Results

This document presents a mathematical modeling framework for COVID-19 at Cornell. The framework is designed to support decision making for university leadership as they consider whether and how to bring students back for a residential fall semester, and as they monitor and support Cornell’s May/June research reactivation. It is not intended to support decisions about how to initiate research reactivation, as those decisions are moving on a faster timeline. This section is intended for a broad audience and provides an overview of the methods and results. Later sections go into much more detail.

**Goals and Non-Goals:** This document’s primary goal is (1) to describe the modeling framework so that it can be vetted before using it to support decisions; (2) to describe the modeling work that remains to support conversations about which work should be prioritized; and (3) to understand which parameters are most influential so that we can prioritize data collection and other parameter estimation efforts. Toward these goals, it also shows results from the current implementation. These results are likely to change as we obtain more accurate parameter estimates and improve the model, but we are becoming more and more confident in the predictions herein.

We emphasize again that this document should **not** in its current form be interpreted as our best and final prediction for what will happen. That is still a work in progress. Indeed, large differences in results across parameter scenarios sensitivity analyses below show that estimates for outcomes are sensitive to parameters. Moreover, while each sensitivity analysis plot shows the sensitivity to only one parameter as we hold the others fixed at nominal values, in reality our estimates may *all* need adjustment simultaneously, potentially by quite a bit for some parameters. As a result, while a strategy may be robust to errors in a single parameter, it may not necessarily be robust to the full uncertainty we face. In addition to uncertainty about parameters, additional uncertainty is introduced by the need to make structural assumptions about the world that do not hold in reality. Hence, with our current knowledge, we are only moderately confident in our ability to say whether a particular strategy will work or not work in achieving a desired level of risk. Instead, we think of this document as a step along a road toward a robust and nimble strategy.

**Simulation Methodology:** The modeling framework, described in detail below, uses a stochastic population-level simulation that models the number of people in each of a number of states over time. States describe the course of the disease over time in an individual in a detailed way that builds on a standard SEIR epidemic model; see, e.g., Li et al. (1999) with random durations in disease states. To this SEIR backbone our model adds more detailed accounting of when an individual becomes PCR positive, includes asymptomatic but infectious individuals, and models how an individual’s age influences the severity of their symptoms.

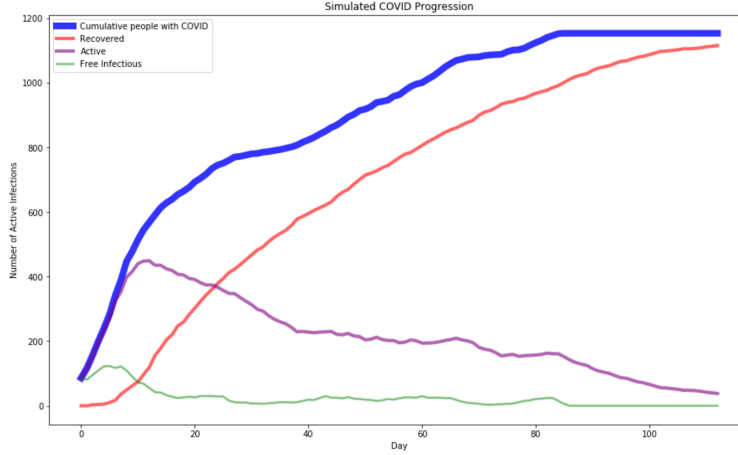


Figure 1: An example trajectory from our simulation, for the fall semester with asymptomatic testing and nominal parameters. The simulation begins with 0.25% of the population (85 people) who are infected and unknown to health authorities. People who are infected but would have been identified in “return to campus” testing are not pictured. As they infect others, the number of active infections (purple line) grows. At the same time, many of these infectious cases are identified through asymptomatic screening, symptomatic self-reporting, and contact tracing, and then quarantined or isolated. This causes the number of free infectious people (green line) to be smaller than the number of active infections. The number of free infectious individuals initially rises but then slowly shrinks, representing the net effect of new infections and quarantine/isolation. Active infections initially rise and then shrink as people enter a recovery phase (red line). The blue line represents the total number of people who have been infected at any point. Eventually, all active infections are quarantined or isolated. At this point in the simulation the number of cumulative infections ceases growing because infections from outside sources are not modeled. Adding the capability to simulate outside infections is in progress. This figure represents only one trajectory under the simulation — because of randomness, outcomes vary from trajectory to trajectory, and a better measure of aggregate outcomes is given by the histograms in Figure 3.

Individuals that report symptoms are tested and isolated, resulting in contact tracing and quarantining identified contacts. Asymptomatic surveillance is also conducted and positive cases found have contacts traced. We also include a parameter that controls how many contacts a person has per day and the rate of infection for each contact. This allows including the impact of social distancing and other transmission mitigation measures like masks if their effects on contacts and transmission can be modeled. The impact of surveillance upon return to campus at the start of the fall semester can be modeled through an initial prevalence parameter.

With one replication the model generates one possible future. An example of the result of one such replication is shown in Figures 1 and 2. Many replications yield ensemble forecasts of the future, as discussed below in Preliminary Results and illustrated in Figure 3.

While we believe that this simulation model captures most phenomena determining growth of a COVID-19 epidemic, like any model it has several limitations. Moreover, due to the need to deliver answers quickly, an explicit decision was made to accelerate development through carefully

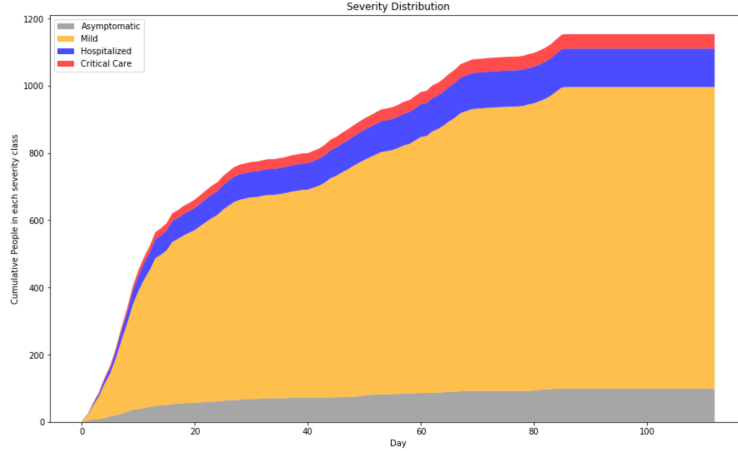


Figure 2: For the same trajectory as Figure 1, cumulative infections that have passed beyond the timepoint when they would become symptomatic, broken out by severity of symptoms, versus the number of simulated days. Grey represents individuals that remained asymptomatic through the course of their infection, orange represents individuals whose worst severity was mild, blue represents individuals that required hospitalization but not critical care, and red indicates individuals that required critical care. The number of people represented at any given point in this figure is slightly smaller than the cumulative number of people with COVID in Figure 1 (most visible on day 0) because it does not include people who are early in their disease and have not yet reached the time point when they would become symptomatic.

considered approximations in two key aspects: contact tracing and risk groups. This is discussed in detail below in a subsection on limitations.

**Parameters:** We obtain parameters from the literature. Unfortunately, the literature is fragmented with an incomplete understanding of several important aspects of disease dynamics. Our work continues to refine parameter estimates using data from the literature, the Tompkins County Health Department, and from Cornell (for contact rates, fraction of the population in high-risk groups). Where it is not possible to narrow down the value of important parameters, we explore the impact of the parameter over a plausible range. Parameters are discussed in detail in Section 2.

**Contact Tracing and Testing Upon Return:** In all scenarios, we assume that contact tracing is performed on individuals that test PCR positive, whether these individuals were identified through self-reported symptoms or asymptomatic surveillance.

We do not study the impact of surveillance through PCR testing immediately upon return to campus explicitly, but the value of such surveillance can be studied through the choice of initial prevalence. By screening students when they return to campus (and, optionally for some, before they leave home), we can reduce the initial prevalence among the non-isolated campus community.

We do not currently consider antibody tests because of the lack of clarity surrounding their accuracy and the elevated risk of noncompliance associated with a blood test instead of a saliva-

based test. At the same time, one can imagine their use for better measuring prevalence and disease progression.

**Asymptomatic Screening with Group Testing:** In the fall semester (but not for the May/June research reactivation), we propose and study the use of regular asymptomatic screening of the Cornell population. When applying asymptomatic testing in our baseline setting, we test 1/14 of the entire campus population every day. Each member of the campus population is then tested once every 2 weeks. We also include a sensitivity analysis examining the effect of more and less frequent screening.

Feasibility and cost-effectiveness of this frequency of testing is likely to require group testing, discussed in detail below in Section 5. There we discuss ongoing work to develop a group testing protocol in collaboration with Drs. Diego Diel and Jeff Pleiss. This requires regulatory approval for group testing at the ADHC. Work is underway to enable this.

While laboratory work must be conducted to estimate sensitivity and specificity parameters that would inform a protocol design, we describe there one design that could plausibly achieve a false negative rate of 19% (among individuals at a post-exposure timepoint in their disease typically detectable in individual PCR) using less than 400 PCR tests per day to test 1/14th of the Cornell community per day. Estimates that are somewhat optimistic but are nonetheless plausible place the weekly cost of materials and supplies for laboratory tests at a perhaps surprisingly low \$3,400/week. This does not include the costs of sample collection (labor, transportation, tubes, viral transport media) or labor to operate the tests, and so the real costs are likely to be significantly larger. The cost of labor for sample collection could perhaps be mitigated by asking members of the community to collect their own saliva using spit kits.

While we study a simple fixed screening strategy in which all members of the campus community are tested equally often, we envision that there is significant value in testing in a more targeted way: e.g., testing all residents of a dorm floor when one resident tests positive; testing those with more contacts or more frequent contact with high-risk individuals; testing a dorm based on the results of PCR analysis of wastewater.

**Scenarios Analyzed:** We use our methodology to analyze two scenarios:

- Cornell’s Summer Research Reactivation: in which the campus population will expand from roughly 1500 to roughly 2500. At this time, asymptomatic surveillance will not be available.
- Cornell’s Fall Semester: Bringing a substantial portion of the student body back to Cornell’s Ithaca campus in the fall semester, either with or without asymptomatic testing.

Although we do not plan to use this modeling framework to support decision-making about the summer research reactivation, we include it as a useful baseline. By observing symptomatic reporting, the results from contact tracing, and other metrics following research reactivation, we gain more understanding of the likely value for key parameters used in our modeling approach. This data can then be used to adjust parameter estimates and perhaps adjust decision-making.

While we study a fixed asymptomatic screening frequency, with transmission rates and number of contacts per day corresponding to fixed social-distancing measures, we underscore the need to be nimble and react to facts on the ground. We envision that one would monitor prevalence based on results from asymptomatic screening and would then adjust the screening frequency and social distancing measures to control the virus while also reducing costs and support an enjoyable campus life.

**Performance Measures:** As our primary outcome measure we examine the expected number of members of the Cornell community that undergo serious negative health effects from COVID-19 requiring hospitalization by the end of the simulated period of 16 weeks (112 days). This simulated period is used for both the May/June and Fall settings and is chosen to be roughly equivalent to the length of the fall semester. While the remaining time in the summer from the start of the May/June reactivation is less than 16 weeks, we use the same time length as the fall to support comparison between the two parameter settings. We also report 10% and 90% quantiles of this performance measure, reflecting the range of potential futures our simulation model produces under the nominal choice of parameters. We use Monte Carlo simulation with 500 replications for each scenario. The use of Monte Carlo simulation creates some errors when estimating these outcome measures, which could be reduced by running more simulation replications. The bulk of the uncertainty arises from uncertainty about parameters and the structure of the simulation model itself rather than from Monte Carlo error.

In interpreting these outcomes, it is important to emphasize that the counterfactual risk of *not* increasing the on-campus population is not 0: those that do not come to campus may face significant risk at home.

**Summary of Preliminary Results:** We first run a simulation under a nominal set of parameters for the three scenarios described above (May/June; Fall with and without asymptomatic surveillance), described in detail in Section 2. We also consider two other sets of parameters, one more optimistic than the nominal parameters and one more pessimistic.

Since our model produces random potential futures, the outcome variable is also random. Figure 3 shows histograms of the Fall outcome (fraction of the population hospitalized) across multiple replications with and without testing under the three different sets of model parameters:

For sensitivity analysis, for each of several parameters we run other simulations varying that single parameter while holding the other parameters fixed at their nominal values. An example plot (Figure 4) shows how our outcome variable (percentage of the population requiring hospitalization due to COVID-19) varies with one of the parameters in our model. The plot shows the estimated median, 10% quantile and 90% quantile of the percentage of individuals requiring hospitalization vs. one of the parameters in our model: the probability that a symptomatic individual reports their symptoms on a given day. When an individual is more likely to self-report symptoms, infectious cases are identified, isolated, and contact traced sooner, resulting in better control of the disease.

Plots are shown for three scenarios: the May/June research reactivation (orange, without asymptomatic testing); and a fall reopening with and without asymptomatic testing (green and blue respectively). In the fall, we model students as having more contacts, which causes a greater risk. This risk can be partially mitigated through asymptomatic surveillance. A full complement of these plots are given in Section 3.

In examining these plots, we emphasize the sensitivity of the outcomes to parameters. Moreover, in Figure 4 and other figures in Section 3, only *one* parameter is varied. If one varies multiple parameters simultaneously, as we do in Figure 3, then one can see even larger changes. The key lesson is that parameter estimation and understanding the region of parameter space we are likely to confront in the fall is essential. We are actively working on these goals.

**Current Limitations of the Simulation Model:** While we believe that our model captures most aspects of the real world that play a first-order role in the growth or control of a COVID-19 epidemic, there are several aspects we do not model that may materially alter the results.

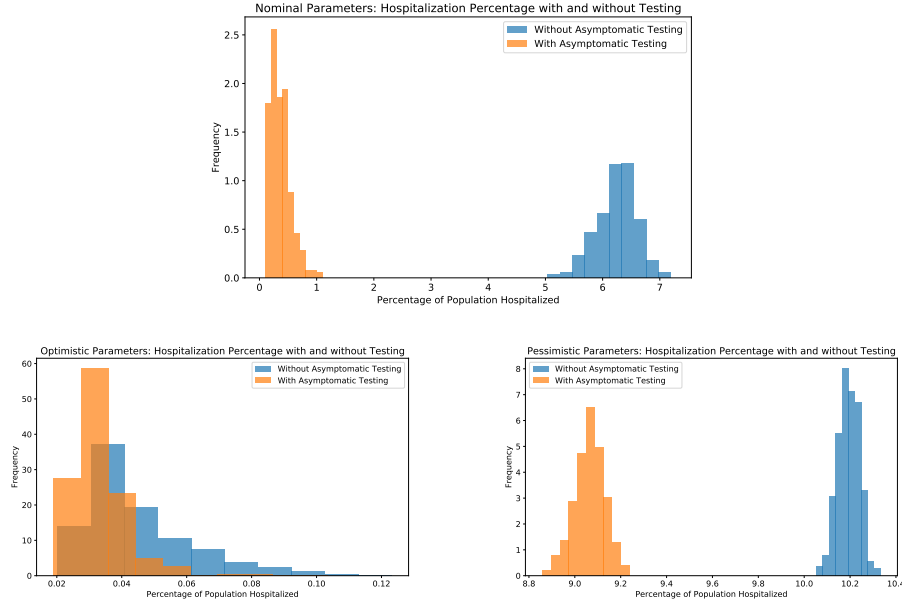


Figure 3: Histograms showing the number of hospitalizations in the fall semester with and without asymptomatic surveillance. Top shows histograms under a nominal set of parameters. Bottom shows two alternate sets of parameters: one that is more optimistic than the nominal parameters, and another that is more pessimistic. Predictions vary significantly as we modify parameter settings.

1. Interactions are assumed to be homogeneous across the entire Cornell population and no local community structure such as friendship networks or different interactions for faculty or staff compared to students is assumed or leveraged. Accounting for this may influence outcomes since we anticipate higher contact rates among students vs. staff/faculty may lead to higher infection rates in students and lower rates in staff/faculty. This may reduce the number of severe infections, since high-risk individuals are more concentrated among faculty and staff.
2. In our model, infectiousness does not vary once the infectious period begins, i.e., once the initial exposure period ends.
3. Infectiousness does not vary across individuals: mild cases are assumed to be just as infectious as severe cases. Similarly, after a person becomes infectious, their infectiousness does not vary over time. In reality, asymptomatic cases are less infectious than infectious ones, which may reduce the impact of undetected asymptomatic individuals infecting others.
4. We do not model Tompkins County more broadly and its interaction with Cornell, nor do we model travel outside of the area. In particular, no cases are imported from outside, nor do any cases spread beyond the modeled Cornell community.
5. The model of contact tracing is imperfect: within the context of a population-level simulation model, it is difficult to model contact tracing in a way that is robust across a wide range of

parameter settings. For example, we model contact tracing by supposing that the contacts quarantined are all in the pre-infectious exposed state (if enough such individuals exist). This is likely accurate for small contact tracing delays (and we believe that in reality these are small), but becomes inaccurate for large values. More work is needed (see Section 6) to understand and improve the accuracy of our model of contact tracing.

6. We model the impact of age in an imperfect way: the distribution of demographics among infected individuals is modeled as being the same as in the overall population, despite the fact that susceptibility and prevalence among one’s contacts may vary with age.

Several of the limitations are addressable given more time, as discussed in Section 6.

In addition, the simulation model is only as accurate as the parameter estimates it uses. While it is possible to estimate some parameters reasonably accurately, significant uncertainty remains about others. Sensitivity analysis plots in Section 3 give some information about the influence of key parameters on outcome metrics. Within Section 6, we call out ongoing workstreams aimed at better estimating important parameters. We also hearken back to the need to be adaptive: by modifying our strategy (especially, asymptomatic surveillance) based on up-to-date information, we can hope to create a strategy that is robust to parameter uncertainty.

## 2 Parameters

This section describes the parameters used within our simulation model. For each parameter we have chosen a nominal (baseline) value, based on the literature or data where possible. Under our nominal setting, most parameters have a constant value across the scenarios we consider (May/June research reactivation; Fall semester with and without asymptomatic surveillance). Some parameters such as contacts per day per person will rise in the fall as the population density on campus rises and there is a larger fraction of students. Beyond the nominal set, we also consider two other sets of values that represent optimistic and pessimistic scenarios.

We begin by discussing parameters that describe the progress of disease in an individual in Section 2.1, then epidemiological parameters that describe the disease and its spread at a population level along with our interventions in Section 2.2. Section 2.3 discusses contact tracing and Section 2.4 discusses how symptom severity is modeled. Section 2.5 supplies a calculation of the  $R_0$  value implied by a particular parameter setting, to support comparisons to the literature. We finally summarize nominal values and state optimistic and pessimistic parameter settings for each scenario in Section 2.6.

### 2.1 Individual Disease Progression

Our simulation assumes that the disease progresses through several stages in each infected individual, represented in Figure 5.



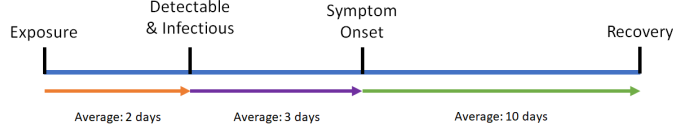


Figure 5: Timeline of disease progression in an infected individual.

Here, during the period after exposure, the individual is infected but the infection is not yet detectable in a PCR test and it cannot yet infect another person. After this exposure period, the individual becomes infectious and detectable by PCR but is not yet symptomatic. Then, after an additional period of time, the individual enters a symptomatic period. During this period, the severity of their symptoms falls into one of two groups: either an extremely mild set of symptoms that the patient would not notice (we refer to this briefly as being “asymptomatic”); or a more noticeable and perhaps even severe set of symptoms (we refer to this as being “symptomatic”). Individuals who are symptomatic self-report their illness to a healthcare provider with a given probability each day while individuals who are asymptomatic do not self-report.

Parameters for the length of these windows are given in Table 1.

Table 1: Parameters for disease progression in an individual.

Parameter Description	Nominal Parameter Value(s)	Sources
Time from exposure to detectable & infectious	Poisson(2)	Lauer et al. (2020); Tindale et al. (2020); Arons et al. (2020); WHO (2020a)
Time from detectable & infectious to symptom onset	Poisson(3)	
Time in symptomatic state	Poisson(12)	WHO (2020b)
P(self-report each day   asymptomatic)	0	
P(self-report each day   symptomatic)	0.8	

Choice of time in the “exposed” and “detectable and infectious” states: Lauer et al. (2020) does a pooled analysis and finds the median incubation period to be 5.1 days, with a confidence interval of 4.5 to 5.8 days. WHO (2020a) and Tindale et al. (2020) find that transmissions can occur 2-3 days before symptom onset. Thus we set the time in the detectable and infectious state to be Poisson(3), and subtract it from the incubation period to get a mean of 2 days for the exposed state.

## 2.2 Epidemiology and Intervention Measures

Next we examine the parameters for epidemiology (how the disease spreads through people’s daily interactions) and intervention measures other than contact tracing (asymptomatic testing and isolation/quarantine). The parameter values are presented in Table 2.

Table 2: Parameters for epidemiology and intervention measures.

Parameter Description	Nominal Parameter Value(s)	Sources
Initial prevalence	0.25%	
Contacts per day (for each non-quarantined/isolated person)	15 (May/June), 20 (Fall)	
P(infection transmission   susceptible -infectious contact)	2.6%	Luo et al. (2020)
Testing false negative rate	0.19	Kojima et al. (2020); Fang et al. (2020); Yang et al. (2020); see Section 5 for explanation
Testing false positive rate	0.005	
P(an isolated individual recovers each day)	0.05	
P(a quarantined individual is released each day)	0.3	

### 2.3 Contact Tracing

In our simulation, each positive case identified through symptomatic self reporting or asymptomatic screening initiates a contact trace. It assumes that each such contact trace results in a deterministic number of contacts identified by the health department. We take this number to be 7 based on data from the Tompkins County Health Department (McMullen, 2020). All such contacts are modeled as either quarantined or isolated.

We also assume that, among these cases quarantined or isolated, the number that are infectious is deterministic given the reason for contact trace initiation: symptomatic self-reporting; or asymptomatic screening. Traces resulting from symptomatic self-reporting are modeled as having a higher number of infectious cases among those contacts identified by the health department because these cases will tend to have been infecting others for a longer period of time.

We assume that contact traces are not initiated for cases isolated as a result of other contact traces. The Tompkins County Health Department does not currently test contacts and so would not know that a contact was positive. Moreover, while a quarantined case could become symptomatic and initiate a contact trace, the fact that this individual had been in quarantine or isolation would dramatically reduce the number of contacts they would have had. The assumption that contact tracing is not done on positives that result from another contact trace nevertheless present a limitation because in the fall additional testing might be performed on contacts.

Here we describe the computation of the two undiscussed contact tracing parameters: the number of infectious cases identified per symptomatic self-report and the number identified per positive identified with asymptomatic screening.

For each positive case newly identified because of self-reporting, we assume that the individual had  $n$  contacts while they were infectious but before they were isolated, where the number of contacts  $n = ct$ , where  $c$  is the average number of contacts per day and  $t$  is the average time a person was infectious before self reporting. (Here, we use the term “contact” in the sense of potentially leading to an infection, rather than the more restrictive sense required by the Tompkins County Health Department for quarantine.)

Given that the individual self-reported, they must be symptomatic (since the asymptomatic self-reporting rate is assumed to be 0), and so  $t$  is the sum of the means of the time in the infection & detectable state (“ID”, below) and the time in the symptomatic state. (Under our nominal parameters, this is  $3 + 1/.4 = 5.5$  days.)

As described above, each contact is assumed to be infected with probability  $p$ , the transmission probability from an interaction. We assume that the process of recalling contacts, and in particular the infected contacts, is imperfect: each infected contact is recalled with a probability  $r$  (the infected contact recollection probability). In total, then the expected number of contact-traced infected contacts is  $N = ctrp$ . We model the actual number of contacts traced as deterministic and equal to this value. All of these identified and positive cases go into isolation (QI). They are pulled from the E, D, and ID states, in that order of precedence.

The remaining  $7 - N$  cases quarantined are pulled from the susceptible (S) state and enter quarantine (QS).

Note that  $ctr = 20 \times 5.5 \times 0.5 = 55$  contacts is much larger than 7 under our nominal parameters: This is because 7 models only those contacts that meet the more stringent guidelines required for quarantine while  $ctr$  is the larger number of contacts that could potentially result in transmission.

Positive cases identified through asymptomatic surveillance follow a similar contact tracing process, but with a smaller number of infectious contacts identified because individuals identified through screening should tend to be identified earlier in the course of their disease at which point they would have infected fewer people. A parameter less than 1 determines the ratio of infectious contacts identified through a positive identified by asymptomatic screening to those identified by a symptomatic case.

Our model of contact tracing has a number of limitations. Perhaps the most important is that it may not accurately capture the expected number of *new* infectious contacts identified through each contact trace. In particular, an infectious contact recalled may have already been identified (through symptomatic self-reporting, asymptomatic screening, or another contact trace) by the time the trace is completed.

Table 3: Parameters for contact tracing.

Parameter Description	Nominal Parameter Value(s)	Sources
Fraction of contacts identified and traced	0.5	
# Quarantined/Isolated per Contact Trace	7	McMullen (2020)
Contact tracing delay	1 day	McMullen (2020)
(Isolations per screening positive) / (Isolations per self-report)	0.5	
(Implied) New Isolations per Self-Report Contact Trace	1.1 (May/June) 1.4 (Fall)	Calculation in text

## 2.4 Severity of Symptoms

Our simulation model separates symptomatic from asymptomatic individuals. Over the course of the simulation, symptomatic individuals self-report each day with some probability, while asymptomatic individuals do not self-report. Symptomatic infections can be of different levels of severity, ranging from mild pneumonia symptoms to critical life-threatening conditions. More granularity in the symptomatic group would give us a better understanding of the simulation outcomes. Thus we

further divide the symptomatic individuals into three different severity levels. In total, we consider four different severity levels, defined as follows:

- Severity level 1: patient is asymptomatic.
- Severity level 2: patient shows mild symptoms, but does not require hospitalization.
- Severity level 3: patient needs to be hospitalized, but does not require intensive care.
- Severity level 4: patient requires intensive care.

At the end of each simulated period, we allocate the symptomatic individuals to severity levels 2-4 with certain proportions. These proportions are estimated from data and are explained in detail below. Though our model does not explicitly assign a severity level to each individual, it does operate under the assumption that individuals do not transition between severity levels throughout the progression of their disease.

Let  $S(\text{severity } i)$  denote the fraction of the population that occupy severity level  $i$ . Then the sum of these severity fractions is the fraction of infected individuals within the overall population. We can use this severity level stratification to express the probability that an infected individual is symptomatic or not. To that end,

$$\begin{aligned} S(\text{asymptomatic}) &= S(\text{severity } 1) \\ S(\text{symptomatic}) &= S(\text{severity } 2) + S(\text{severity } 3) + S(\text{severity } 4). \end{aligned} \quad (1)$$

The probability that an infected individual is symptomatic is then

$$P(\text{symptomatic} \mid \text{infected}) = \frac{S(\text{symptomatic})}{S(\text{asymptomatic}) + S(\text{symptomatic})}. \quad (2)$$

The distribution over severity levels varies significantly with age. Thus, we develop the following age-stratified formula to calculate the fraction of the population within each severity level.

$$S(\text{severity } i) = \sum_{\text{age } j} P(\text{severity } i \mid \text{infection, age } j) \cdot P(\text{infection} \mid \text{age } j) \cdot P(\text{age } j). \quad (3)$$

**Severity Calculation Part 1: Severity and Infection given Age** Parameters for the first two factors in this expression are given in Table 4. The age distribution is specific to the application scenario. We compute the age distribution on Cornell’s campus for the May/June reactivation and fall reopen scenarios below.

Table 4: Parameters for age-stratified infection probability and severity level distribution. Sources: Luo et al. (2020); China CDC (2020); Dong et al. (2020); CDC COVID-19 Response Team (2020); Li et al. (2020).

	Age group 1 (0-17)	Age group 2 (18-44)	Age group 3 (45-64)	Age group 4 (65-74)	Age group 5 (75+)
P(infection   age)	1.8%	2.2%	2.9%	4.2%	4.2%
P(severity 1   age)	10%	7%	7%	7%	5%
P(severity 2   age)	89%	80%	76%	70%	55%
P(severity 3   age)	1%	10%	10%	13%	20%
P(severity 4   age)	0%	3%	7%	10%	20%

In Table 4, the probability of infection given age is taken from Luo et al. (2020), which reports the probability of infection through a close contact for different age groups among 4941 close contacts traced from early cases in Guangzhou, China. The severity level distribution is estimated from a combination of data sources. We begin with the statistics provided by CDC COVID-19 Response Team (2020) on hospitalization and ICU admission rates by age, computed from US data from February 12 to March 16, 2020. By our definition, hospitalization includes both severity levels 3 and 4, and ICU corresponds to severity level 4. The CDC data were taken before the widespread implementation of social distancing in the US. This could be biased since many less severe cases might have been undocumented, making the hospitalization rates appear higher than in reality. Li et al. (2020) estimates that after travel restrictions and social distancing were put in place, about 65% of the cases were documented. Thus, we multiply the CDC estimates by 65% to achieve the  $P(\text{severity } 3, 4 \mid \text{age})$  estimates above.

To construct the remainder of Table 4, we then distribute the remaining probability mass between severity levels 1 and 2. China CDC (2020) and Italy’s Istituto Superiore di Sanità (2020) reported an asymptomatic rate of 1.2% and 7.5% among confirmed cases respectively. We adopt the higher estimate from Italy. We start with the assumption that the ratio between severity level 1 and severity level 2 is the same across all age groups and compute this ratio to match the population-level asymptomatic rate to 7.5%, using the US age distribution provided by Central Intelligence Agency (2020) and Kaiser Family Foundation (2018). Then we use this ratio distribute the remaining probability mass between severity levels 1 and 2 for each age group. Next we correct for the variation of asymptomatic rates across age groups. Backhaus (2020) suggests that the asymptomatic rate is higher among younger people, so we decrease the severity level 1 for age group 1 and increase it for age group 5.

We also consider two additional parameter settings, one optimistic and one pessimistic, with smaller and larger asymptomatic fractions respectively. The parameters for those are shown in Table 5. Note that age group 0 is not present on campus in either the May/June or Fall scenarios.

Table 5: Severity level 1 and 2 distributions in two additional settings.

Optimistic setting:					
	Age group 1	Age group 2	Age group 3	Age group 4	Age group 5
$P(\text{severity } 1 \mid \text{age})$	5%	4%	4%	4%	3%
$P(\text{severity } 2 \mid \text{age})$	94%	83%	79%	73%	57%

Pessimistic setting:					
	Age group 1	Age group 2	Age group 3	Age group 4	Age group 5
$P(\text{severity } 1 \mid \text{age})$	15%	10%	10%	10%	5%
$P(\text{severity } 2 \mid \text{age})$	84%	77%	73%	67%	55%

**Severity Calculation Part 2: Age Distribution** To complete our severity calculation, we first identify different groups on Cornell’s campus and estimate their distribution over the five age groups. The parameter values are given in Table 6.

Table 6: Information for different population groups on Cornell’s campus. The size of each group as well as the faculty age distribution are provided by Cornell Institute for Research and Planning (2019); the age distribution for academic professionals, staff, and students are assumed.

	Group size	Age group 1 (0-17)	Age group 2 (18-44)	Age group 3 (45-64)	Age group 4 (65-74)	Age group 5 (75+)
Faculty	1684	0%	33.1%	46.1%	17.9%	2.9%
Academic professionals	1114	0%	90%	10%	0%	0%
Staff	7485	0%	50%	50%	0%	0%
Students	24027	0%	100%	0%	0%	0%

In the May/June reactivation scenario, we use a total population size of 2500. This is based on an assumption that there are 1500 people on campus before the lab restart, and that roughly 1000 people would come back to campus after the restart. These assumptions were based on an email from Gary Koretzky to Peter Frazier on May 10. For the Fall reopen scenario, we use a total population size of 34,310, based on Cornell’s total population as of Fall 2019, compiled in the University Factbook by Cornell Institute for Research and Planning (2019).

The next step is to determine the age distribution for the two scenarios. This is important for computing the population-level severity statistics, as outlined in Equation 3. For the May/June reactivation, we assume there are 150 undergraduates based on a conversation between Gary and Peter in early May. The remaining 2350 people are assumed to be faculty, academic professionals, staff, and PhD students. We use the “faculty / academic professional / staff / PhD” ratio in Table 6 to extrapolate the distribution over 2350 people and estimate there to be 293 faculty, 194 academic professionals, 1302 staff, and 561 PhDs. Then we use these numbers to compute a combined age distribution over 2,500 people. For the fall reopen, we assume everyone is on campus and compute a combined age distribution over all 34,310 people. Results are presented in Table 7.

Table 7: Parameters for age distribution on campus for May/June reactivation and Fall reopen.

	Age group 1 (0-17)	Age group 2 (18-44)	Age group 3 (45-64)	Age group 4 (65-74)	Age group 5 (75+)
P(age) for May/June reactivation	0%	65.34%	32.22%	2.10%	0.34%
P(age) for Fall reopen	0%	85.81%	13.17%	0.88%	0.14%

Finally, using the age distributions for the two scenarios, we can calculate the severity level distributions using Equation 3. Results are presented in Table 8.

Table 8: Severity level distribution on campus for May/June reactivation and Fall reopen under the nominal scenario.

	Severity 1	Severity 2	Severity 3	Severity 4
May/June reactivation	6.99%	78.42%	10.10%	4.49%
Fall reopen	7.00%	79.35%	10.04%	3.61%

## 2.5 Implied $R_0$

To support intuition and comparison to other measurements of disease spread, it is useful to calculate the  $R_0$  implied by a fall scenario with no testing or contact tracing measures. In this scenario, infected individuals are only isolated if they self-report. We estimate  $R_0$  under optimistic, nominal, and pessimistic parameters.

First, we find the expected time that a case is both infectious and free. This is the sum of the duration of the infectious period before symptom onset (time in ID) and the expected time of being free after symptom onset (time in Sy). For asymptomatic individuals, the latter is the remaining length of their disease duration because they do not self-report. For a symptomatic individual, who self-reports every day with a fixed probability, the expected number of days that he/she is free after symptom onset is given by inverse of his/her daily self-reporting probability. Then, over each day in the “infectious and free” duration, a free infectious individual comes in contact with a certain number of people and infect them with a fixed probability (2.6% in all three scenarios). Thus, the expression for  $R_0$  is given by

$$\begin{aligned} & (\text{Days infectious pre-symptoms} + \text{Expected days free post-symptoms}) \\ & \quad * \text{Contacts / day} * \text{Probability (infection transmissions | contact)}, \end{aligned}$$

where

$$\begin{aligned} \text{Expected days free post-symptoms} = & \text{percent asymptomatic} * \text{duration of Sy} \\ & + \text{percent symptomatic} * 1 / \text{daily self-reporting probability}. \end{aligned}$$

For the three parameter settings, we calculate  $R_0$  according to the procedure above:

- Optimistic:  $R_0 = (2.5 + (4\% \cdot 10 + 96\% \cdot 1/60\%)) \cdot 15 \cdot 2.6\% = 1.755$ .
- Nominal:  $R_0 = (3 + (7\% \cdot 12 + 93\% \cdot 1/40\%)) \cdot 20 \cdot 2.6\% = 3.2058$ .
- Pessimistic:  $R_0 = (3.5 + (10\% \cdot 14 + 90\% \cdot 1/20\%)) \cdot 25 \cdot 2.6\% = 6.11$ .

Note: These numbers might be slight over-estimates because the above calculation assumes that all people an infected person comes into contact with are *distinct*. In reality, a person is likely to have common contacts on different days. Moreover, the contacts of different people might overlap given the small-world network structure of Cornell’s campus, as studied by Weeden and Cornwell (2020), which notes the tight clustering and low degrees of separation among students based on course co-enrollment information alone. Note  $R_0$  is calculated under the assumption that all others are susceptible.

## 2.6 Nominal Parameter Values for May/June Reactivation and Fall Re-open

In addition to the nominal parameters, we consider an optimistic and a pessimistic setting. Table 9 is a comprehensive summary of the parameters we use for all settings.

Table 9: Parameters for optimistic, nominal, and pessimistic settings.

Parameter Name	Optimistic	Nominal	Pessimistic
Time in E	Poisson(2)	Poisson(2)	Poisson(2)
Time in D	0	0	0
Time in ID	Poisson(2.5)	Poisson(3)	Poisson(3.5)
Time in Sy (with and w/o symptoms)	Poisson(10)	Poisson(12)	Poisson(14)
Contacts per day (for each free person)	10 (May/June) 15 (Fall)	15 (May/June) 20 (Fall)	20 (May/June) 25 (Fall)
P(infection transmission   susceptible-infectious contact)	2.6%	2.6%	2.6%
Total Population	2500 (May/June), 34310 (Fall)		
Initial Prevalence	0.1%	0.25%	0.5%
Asymptomatic rate	4%	7%	10%
P(self-report each day   no symptoms)	0%	0%	0%
P(self-report each day   symptoms)	60%	40%	20%
Fraction of infectious contacts identified and traced	0.6	0.5	0.4
New Quarantines+Isolations per Contact Trace	7	7	7
(Implied) New Isolations per Self-Report Contact Trace	0.65 (May/June) 0.98 (Fall)	1.1 (May/June) 1.4 (Fall)	1.6 (May/June) 2.0 (Fall)
(Isolations per screening positive) / (Isolations per self-report)	0.5	0.5	0.5
Contact Tracing Delay	0 day	1 day	2 days
Testing false positive rate	0.005	0.005	0.005
P(an isolated individual recovers each day)	0.05	0.05	0.05
P(a quarantined individual is released each day)	0.3	0.3	0.3
Age-severity matrix	Optimistic	Nominal (Table 8)	Pessimistic
$R_0$ in fall w/o intervention	1.755	3.2058	6.11
Simulated time length	16 weeks (112 days)		



### 3 Results

The results below indicate the sensitivity of our model outcomes under small perturbations to meaningful parameters. In each of the Figures below we perturb a single parameter and otherwise fix all other parameters to their default value.

Our first set of sensitivity results compare three default parameter configurations against one another: nominal June reopen parameters, nominal Fall reopen parameters without asymptomatic testing, and nominal Fall reopen parameters with asymptomatic testing. The default value of all relevant parameters for each of these configurations is outlined in Table 9. Our sensitivity plots for these parameter configurations span the following list of parameters:

- The daily likelihood of a symptomatic individual self-reporting (Figure 6). This was also shown above as Figure 4.
- The initial prevalence of the infection, stated as a percentage of the total population (Figure 7).
- The probability of transmission when an infectious individual comes into contact with a susceptible individual (Figure 8).
- The average number of contacts per person per day, for an individual who is not quarantined or isolated (Figure 9).
- The contact trace delay, i.e. the number of days between an individual self-reporting and the resulting quarantine and isolation decisions enacted from that individual's contact trace (Figure 10).
- The number of new positive cases that are identified and isolated for each one individual who undergoes a contact trace (Figure 11).
- The fraction of infections which are asymptomatic (Figure 12).

Our second set of sensitivity plots pertain to asymptomatic-testing-specific parameters, and for these plots we contrast the optimistic, nominal, and pessimistic Fall parameter configurations against one another. All of the default values for these parameters can again be found in Table 9. These sensitivity plots vary the following parameters:

- The percentage of the population that is tested for the infection each day (Figure 13).
- The false-negative rate associated with the daily tests (Figure 14).

Each point on each of the sensitivity plots contained in Figures 6—14 is obtained from 500 Monte Carlo replications for the relevant parameter configuration over a time horizon of 112 days or 16 weeks. We do not indicate the Monte Carlo error in these plots; indeed, the Monte Carlo error tends to be very small, except when estimating very small probabilities. The y-axis corresponds to the distribution of hospitalizations at the end of the 16 week time horizon; the main plot depicts the 50th percentile, while the shaded region depicts the 10-90th percentile range.

The sensitivity plots are included below. Subsequently, in Section 3.1, we include a discussion about important trends and conclusions which can be surmised from these figures.

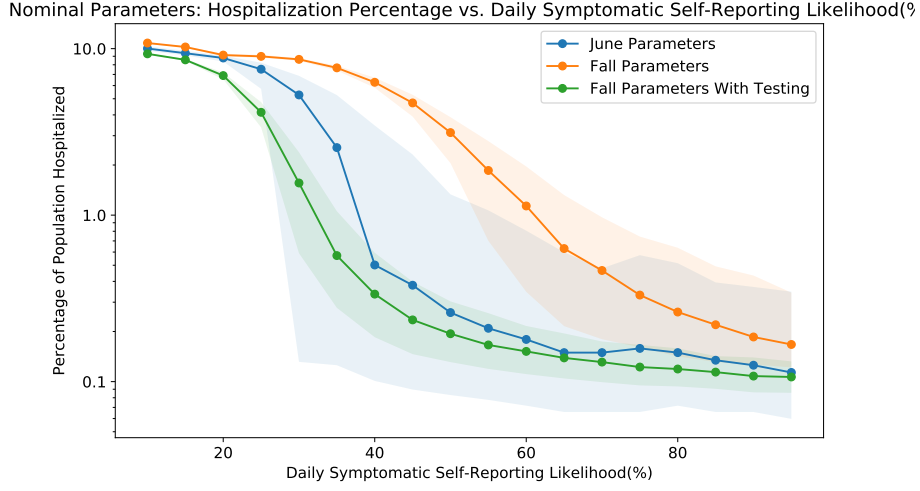


Figure 4: Plot depicts the distribution of hospitalizations (i.e. 50th percentile, with the wider range corresponding to the 10-90th percentile range) vs. the daily likelihood that a symptomatic individual self-reports their infection status. The nominal value of this parameter is 40%, for both the May/June parameters and the Fall parameters, i.e. we assume that symptomatic individuals will exhibit an abundance of caution and diligently self-report the presence of symptoms.

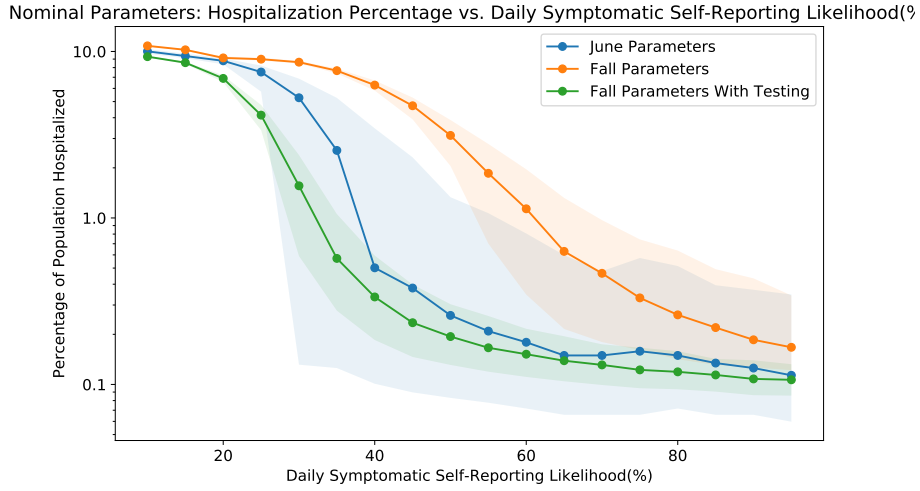


Figure 6: Plot depicts the distribution of hospitalizations (i.e. 50th percentile, with the wider range corresponding to the 10-90th percentile range) vs. the daily likelihood that a symptomatic individual self-reports their infection status. The nominal value of this parameter is 40%, for both the May/June parameters and the Fall parameters, i.e. we assume that symptomatic individuals will exhibit an abundance of caution and diligently self-report the presence of symptoms.

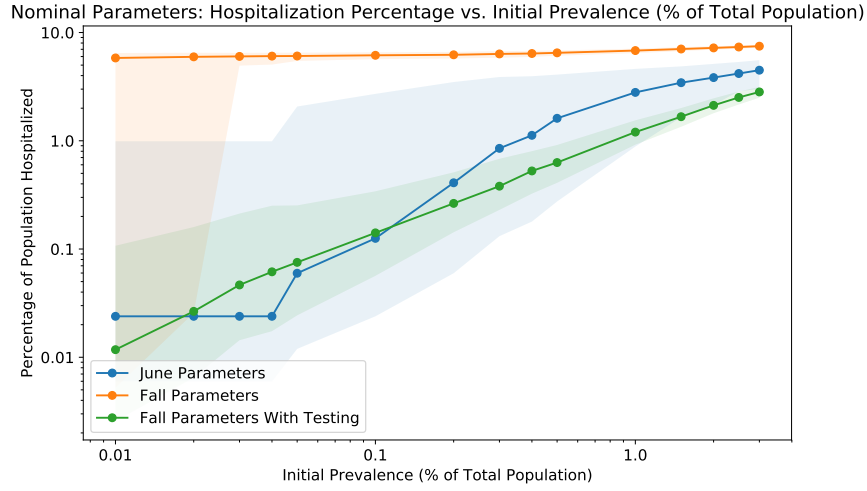


Figure 7: Plot depicts the distribution of hospitalizations (i.e. 50th percentile, with the wider range corresponding to the 10-90th percentile range) vs. the initial percentage of infected individuals within the population. The nominal value of this parameter is 0.25%, for both the May/June parameters and the Fall parameters. This was also shown above as Figure 4.

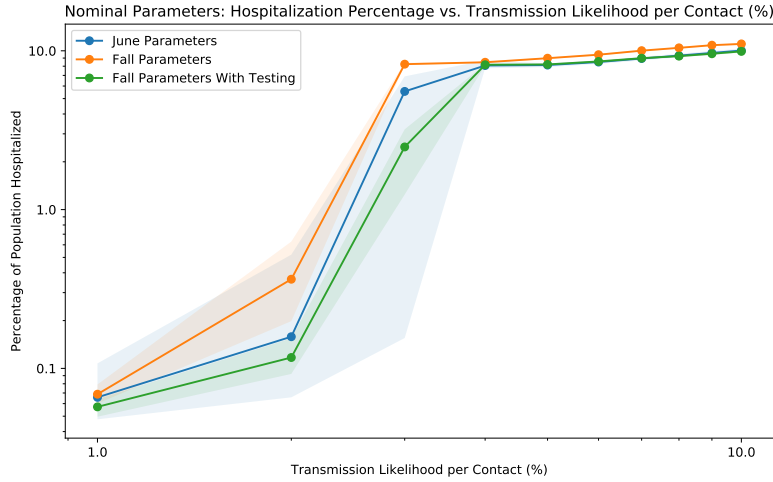


Figure 8: Plot depicts the distribution of hospitalizations (i.e. 50th percentile, with the wider range corresponding to the 10-90th percentile range) vs. the likelihood of transmission when a susceptible individual comes into contact with an infectious individual. The nominal value of this parameter is 2.6%, for both the May/June parameters and the Fall parameters.

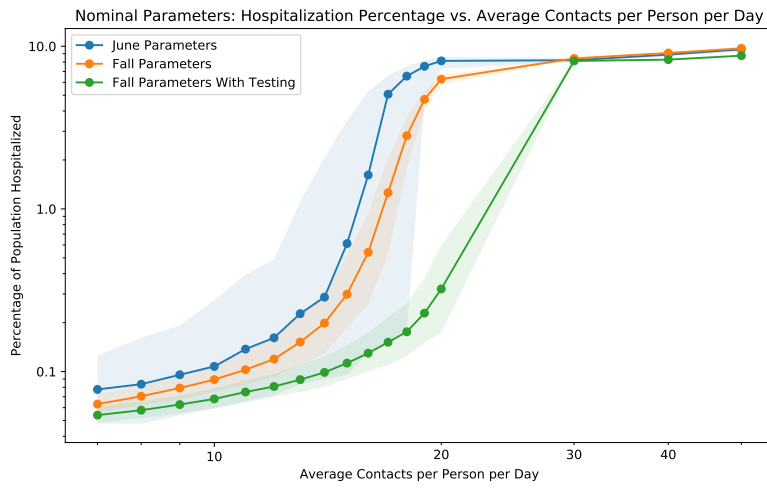


Figure 9: Plot depicts the distribution of hospitalizations (i.e. 50th percentile, with the wider range corresponding to the 10-90th percentile range) vs. the average number of contacts that a non-quarantined an non-isolated individual has on any given day. The nominal value of this parameter is 15 contacts per day, for the May/June parameters, and 20 contacts per day for the Fall parameters.

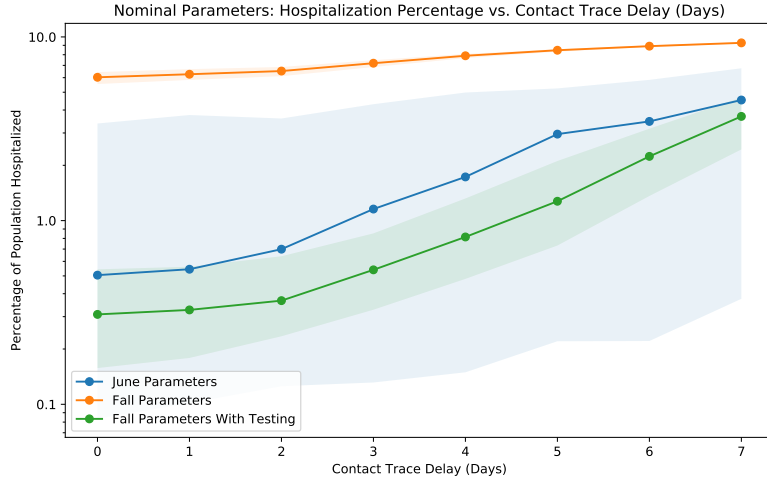


Figure 10: Plot depicts the distribution of hospitalizations (i.e. 50th percentile, with the wider range corresponding to the 10-90th percentile range) vs. the delay, measured in days, from identifying a new positive case to isolating their contacts via contact tracing. The nominal value of this parameter is 1 day, for both the May/June parameters and the Fall parameters. As described in the introduction, we believe that our model of contact tracing becomes less accurate for large contact tracing delays: in reality, at large contact tracing delays, we expect the number of hospitalizations to be significantly larger than what is predicted here. Work to address this inaccuracy is called out in Section 6.

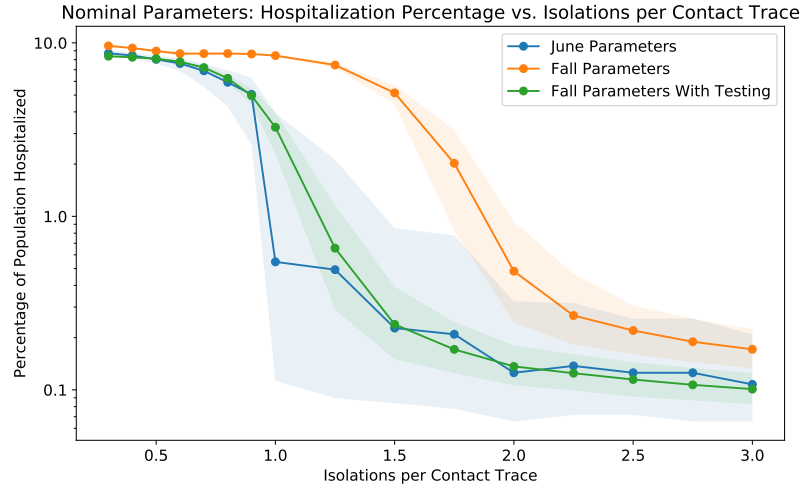


Figure 11: Plot depicts the distribution of hospitalizations (i.e. 50th percentile, with the wider range corresponding to the 10-90th percentile range) vs. the number of isolations which occur for each individual who undergoes a contact trace. The nominal value of this parameter is 1.1 for May/June parameters, and 1.4 for Fall parameters.

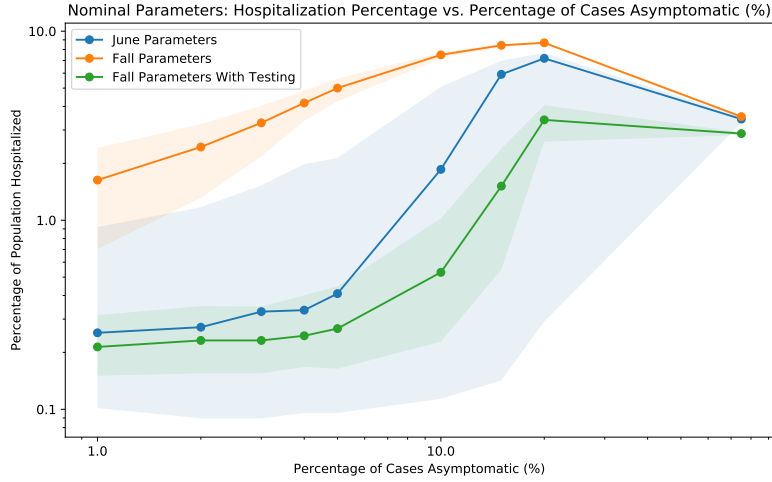


Figure 12: Plot depicts the distribution of hospitalizations (i.e. 50th percentile, with the wider range corresponding to the 10-90th percentile range) vs. fraction of infections which become asymptomatic. The fraction of asymptomatic infections is 4%, 7%, and 10% for optimistic, nominal, and pessimistic scenarios respectively.

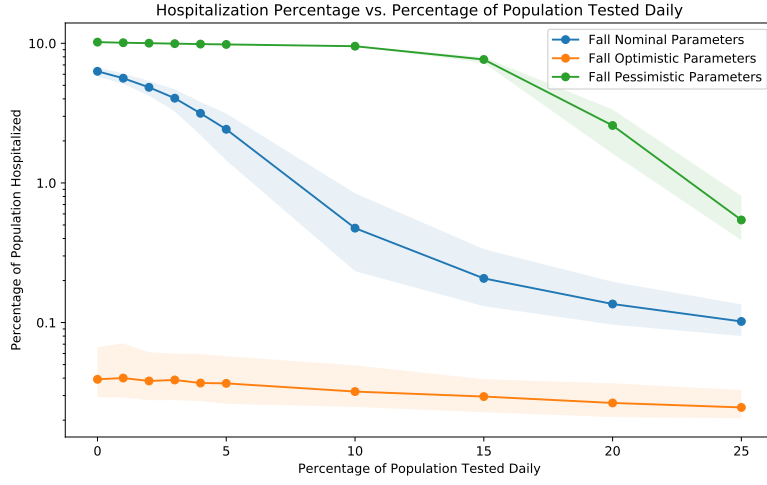


Figure 13: Plot depicts the distribution of hospitalizations (i.e. 50th percentile, with the wider range corresponding to the 10-90th percentile range) vs. the percentage of the total population that is tested for the presence of infection each day. The nominal value of this parameter is 7% of the population, across optimistic, nominal, and pessimistic parameters, which approximately corresponds to testing the entire population once every 14 days.

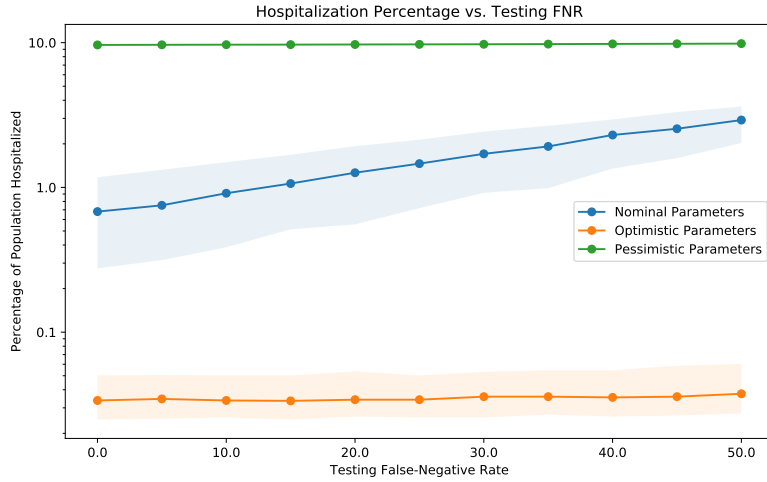


Figure 14: Plot depicts the distribution of hospitalizations (i.e. 50th percentile, with the wider range corresponding to the 10-90th percentile range) vs. the false-negative rate used for the daily testing procedure. The plot is restricted only to the Fall parameters with asymptomatic testing. The nominal value of this parameter is 19% of the population, across optimistic, nominal, and pessimistic parameters.

### 3.1 Results Discussion

First, let us remark that Figure 3 depicts a histogram of hospitalization percentages for all of the fall parameter configurations with and without testing. These histograms provide a useful starting point for interpreting the outcomes depicted in the above figures. In addition, nominal values are contained in each of the above figure captions.

Figures 6, 9, and 12 show quantiles for the fall parameters that may appear surprisingly narrow at a first glance. This is because, for these particular configurations, the parameters cause a very large fraction of the population to be infected. In this case, the variance of the infected fraction of the population is fairly small compared with the variance that occurs in smaller epidemics. (In smaller epidemics, from sample path to sample path, we could easily see a factor of 2 variation in the number of people infected). Moreover, the number of people hospitalized is given by a simple binomial split between symptomatic and asymptomatic, the variance of which is controlled by the central limit theorem, and then a deterministic product with  $P(\text{hospitalization} \mid \text{symptomatic})$ . This, together with the use of the log scale, shrinks the quantiles (both in reality, and even more so to the eye).

In addition, Figure 7 shows a surprisingly small sensitivity of median hospitalizations to initial prevalence for fall without asymptomatic testing. This is because, in settings where epidemics grow, the role of the initial prevalence is largely to get out of a stochastic phase in which random variation in contact tracing can contain an epidemic, and into an uncontrolled growth large-scale epidemic. In this scenario, even small initial prevalences are large enough to create a widespread epidemic.

## 4 Detailed Simulation Model Specification

Our model tracks population-level counts of individuals across multiple relevant states. As in reality, the dynamics are stochastic. We use Monte Carlo simulation to generate many potential futures starting from a random initial state that reflects an initial prevalence.

### 4.1 Population-Level Dynamics

The states across which individuals are tracked, and a short description of the dynamics governing relevant state transitions, are as follows. These dynamics are depicted in Figure 15.

**Susceptible (S)** A *susceptible* person does not carry the virus, is not infectious, and tests negative by PCR. A susceptible (S) person becomes exposed (E) with some probability once he/she comes in contact with someone infectious. We describe the assumptions regarding contacts and transmission in more detail below.

**Exposed (E)** An *exposed* person is infected after previous contact with someone infectious. The person is not yet infectious, detectable, or symptomatic. The person spends a random number of days in the exposed state, and then becomes detectable (D).

**Detectable (D)** A *detectable* person carries the virus, is potentially detectable by PCR, but is not yet infectious. The person spends a random number of days in the detectable state, and then becomes infectious and detectable (ID).

**Infectious and detectable (ID)** An *infectious and detectable* person is infectious, i.e. he/she can generate more exposed cases from the currently susceptible population. The person is



not symptomatic and does not self-report their illness. The person spends a random number of days in the infectious and detectable state, and then becomes either Symptomatic or Asymptomatic (i.e., they will never have symptoms).

**Symptomatic / Asymptomatic** The asymptomatic/symptomatic states are the next stage in the disease for those leaving the infectious and detectable state. Asymptomatic people do not report their symptoms. Symptomatic people who have not yet self-reported or been identified in some other way (contact tracing, screening) self-report to the healthcare system with some probability each day. Self-reported individuals enter the quarantine-infected (QI) state. An asymptomatic or a symptomatic person who does not self-report eventually recovers (R).

**Recovered (R)** The person's disease is no longer infectious. We assume all patients recover and there are no deaths. Indeed, the mortality rate is low and we strive to keep prevalence low, deaths would be exceedingly rare. Recovered patients cannot become susceptible again.

**Quarantine-Susceptible (QS)** The person is put in quarantine by a test decision, or by the outcome of a contact trace, but does not carry the virus. At the conclusion of quarantine a person returns to the susceptible state

**Quarantine-Infected (QI)** Someone with the virus is put in isolation or quarantine by a test decision, a contact trace, or by self-reporting. At the conclusion of isolation the person enters the recovered state.

## 4.2 Daily Infection Dynamics

In our model, susceptible individuals can become exposed to the virus and transition to the exposed state, depending on daily contacts and an infection-transmission probability. A “contact” is an interaction between two people that has the potential for transmission of the infection. The dynamics are governed by five values.

1. The expected number of contacts per person per day ( $c$ ). This is an input parameter.
2. The number of free and infectious individuals, i.e., individuals who have the virus, are infectious, and who are not yet in isolation. The number of free and infectious individuals ( $F_I$ ) is the sum of the numbers of individuals in the ID, asymptomatic and symptomatic states.
3. The number of free and susceptible individuals, i.e., individuals who are susceptible to the disease and not currently quarantined. The number of free and susceptible individuals ( $F_S$ ) is simply the number of individuals in state S.
4. The number of free individuals, i.e. the size of the pool of individuals within which interactions can occur. This pool consists of free and susceptible, free and infectious, exposed, detectable and recovered individuals. Hence the number of free individuals ( $F$ ) is the sum of  $F_I$ ,  $F_S$ , E, D and R.
5. The transmission probability  $p$  that gives the probability of transmission during an interaction between an infectious person and a susceptible person.

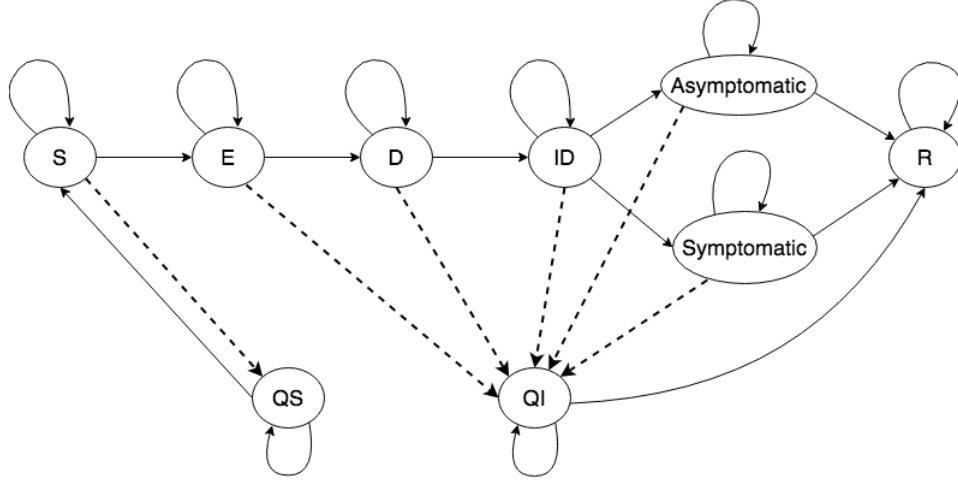


Figure 15: The dynamics between disease and quarantine states over a single time period for the stochastic population-level simulation. “S” = susceptible, “E” = exposed, “D” = detectable, “ID” = infectious and detectable, “Asymptomatic” = in severity group 1, “Symptomatic” = in severity group 2, “R” = recovered, “QS” = quarantined susceptible, and “QI” = quarantined infected. Solid lines represent the epidemiological progressions as well as people being released at the end of their quarantine; dashed lines represent the effects of intervention measures, including testing, self-reporting, and contact-tracing, which put some of the population into isolation/quarantine.

Every infected individual interacts with a random number of other free individuals each day, modeled as a Poisson( $c$ ) random variable. Each of these free individuals is assumed to be susceptible with a probability that is proportional to the number of free susceptibles within the free population, i.e., a contact is a susceptible with probability  $F_S/F$ . Thus, the total number of interactions between an infectious person and a susceptible each day is modeled as a Poisson random variable with mean  $cF_I F_S/F$ . This simplified model of interactions assumes no overlap between the interactions originating from each infectious person. Finally, each interaction between an infectious person and a susceptible person results in transmission with probability  $p$ . Accordingly, the total number of new infections each day is modeled as a Poisson random variable with mean  $cF_I F_S p/F$ .

### 4.3 Interventions: Self-Reporting and Contact-Tracing

There are two interventions through which positive cases can be isolated.

1. Self-reporting. Individuals in the symptomatic state have a probability of self reporting each day. If they self report they enter the quarantine-infected state (QI). If they do not self-report and do not recover, then they remain in their present state for another day.
2. Contact tracing. We use a simplified model of contact tracing. A contact trace is initiated when an individual self-reports symptoms or when they are identified as positive through

asymptomatic screening. Additional contact tracing is not initiated from positive cases found among contacts traced, as the Tompkins County Health Department does not have a policy of testing contacts.

Contact tracing is described by 3 parameters: number of people to place into quarantine or isolation with each contact trace; the number among these that are infectious for self-reporting positive cases; and the number that are infectious for cases identified through asymptomatic screening. We set the number of infectious cases identified smaller for those identified through asymptomatic screening because these cases will tend to have been infectious for less time and thus will tend to have infected fewer people. The choice of these parameters is discussed in detail in Section 2.3.

## 5 Asymptomatic Screening with Group Testing

We envision group testing as an important component for enabling widespread asymptomatic screening. Group testing pools multiple samples together and tests each pool using a single PCR test. It could save a significant amount of testing resources while still ensuring a reasonably high accuracy. The idea of group testing was first proposed by Dorfman (1943) as an approach to screening soldiers for syphilis during WWII. Since then, different group testing protocols have been developed and studied. In the context of COVID-19, recent analyses and editorials Gollier (2020); Kotlikoff (2020); Kotlikoff and Kotlikoff (2020) have called for widespread deployment of group testing because it can greatly expand the testing capacity.

One of the group testing protocols of interest is the square-array protocol, first proposed in Phatarfod and Sudbury (1994) and closely analyzed in Westreich et al. (2008). Under this protocol, we place samples onto a square array and form a pool from each row and each column. A PCR test is run on each pool, providing an indication of whether at least one sample in that pool contains viral material. Samples whose rows and columns are both positive are then either deemed positive or are tested in follow-up confirmatory individual tests. An illustration for a  $5 \times 5$  square array is given in Figure 16.

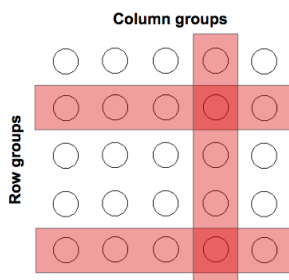


Figure 16: A  $5 \times 5$  square array group test. 25 samples are placed into a  $5 \times 5$  array, divided into five row groups and five column groups. A test is run on each group, totalling 10 tests. Samples at the intersection of positive groups (red) receive individual follow-up tests.

Here we discuss the design of a group testing protocol that would satisfy (or approximately

satisfy) the requirements assumed in this document — an overall FNR of 19% or sensitivity of  $1 - \text{FNR} = 81\%$  — i.e., that a test on an individual in any post-exposed PCR-detectable state is positive with 81% probability. We emphasize that our model assumes that individuals are not PCR-detectable upon exposure and that it takes several days for viral load to grow to the point that their infection would be detectable. We do not require group testing or any other testing methodology to identify individuals in this state.

The sensitivity of a group testing protocol can be estimated using the following formula:

$$\text{sensitivity} = P(\text{sample tests positive in an individual test} \mid \text{it is collected from an infected individual}) \\ \times P(\text{sample tests positive in a group test} \mid \text{it tests positive in an individual test}).$$

The first probability, or namely the sensitivity for an individual PCR test, can be more concretely defined as the probability that the viral load (measured in # copies of viral RNA per unit volume) is beyond the limit of detection (LOD) given that the sample is collected from a PCR-detectable infected individual. Both Kojima et al. (2020) and To et al. (2020) report a sensitivity for the individual PCR test of roughly 90%.

The second probability, or the analytical sensitivity of a group testing protocol is largely driven by dilution effects, which decrease the detectability of individual positive samples in a large pool as the pool grows large, and the robustness of the protocol. Yelin et al. (2020) estimates that the LOD in pooled samples of size 32 is increased to the point that 90% of positive samples that can be detected through individual PCR can be detected through pooled testing. Under the assumption that the viral load in a pooled sample resulting from a given positive individual participate in the pool is the same across pools, we hypothesize that a square-array testing protocol with pool size  $\leq 32$  (in which each sample is included in two pools) has analytical sensitivity of at least 90%. We also note here that more robust protocols (see, e.g., Cheraghchi, 2013) are designed so that they can still identify a positive if one pooled test fails. (Or, in extreme examples, if multiple pooled tests fail.)

Combining the two probabilities mentioned above results in an overall sensitivity of square-array testing protocol of at least 81%.

Experimental measurement of these dilution effects is being conducted by collaborators in the vet school (Dr. Jeff Pleiss and Dr. Diego Diel). In parallel, we are developing predictions for several group testing protocols into whose design we will include experimental data once it is available. Although work is ongoing, initial conversations with Drs. Pleiss and Diel have explored the properties of square array and cubic array protocols with follow-up individual testing on positives. These conversations suggest that, under a square array protocol, the maximum pool size at which we can achieve an analytic sensitivity high enough (i.e., a limit of detection low enough) to achieve a comparable overall false negative rate to an individual PCR test is somewhere between 5 and 100. (Obviously, this is a large range.)

Under a pool size of 24 as recommended by Dr. Pleiss, since each array requires 48 tests which fit nicely on a 96-well PCR plate, and assuming a 1% prevalence level, a  $24 \times 24$  square-array test with individual follow-ups requires 0.13 tests per sample on average, as computed using the group testing metrics calculator (Wan, 2020).

For a total campus population of 34310, testing 1/14 of the population daily means collecting 2451 samples per day. To test roughly 2451 samples per day, we expect to need  $2451 \times 0.13 = 319$  PCR tests per day; This is within the capacity of the Animal Health Diagnostic Center (ADHC).

While the costs to run these tests depend on a number of factors which depend on regulatory conversations and laboratory measurements, Dr. Pleiss estimates that the cost of the group testing

(not including tubes, viral transport media, sample collection, transportation, and IT) would be on the order of 20 cents per sample tested. At the above cadence of 1/14 of the community per day, this would cost roughly \$3.4K per week.

The additional cost of sample collection could be reduced by asking students and other members of the campus community to collect their own saliva (and potentially also add transport media). In particular, one possible implementation of asymptomatic surveillance would follow the following steps, leveraging the capabilities of the ADHC.

- Student (or staff / faculty) gets a saliva RNA collection kit on a bi-weekly basis;
- Student spits into the tube until the saliva sample reaches a specified volume (indicated on the tube);
- Student adds viral transport media (VTM) that comes with the kit to the tube;
- Student sticks the barcode label to the tube and keeps a photo of the label for future reference;
- Student drops off the saliva sample at specified drop-off locations (e.g. first floor of dorm buildings) throughout the campus;
- Courier collects samples (contactlessly) on the same day and brings them to the vet school lab;
- ADHC uses group testing to identify positive cases.

## 6 Ongoing Work

One goal of this document is to solicit feedback on which work should be done next to improve this modeling framework and its usefulness, understanding that each work item takes time and we likely cannot do everything before June 15. Here we provide a table of improvements that we could consider, along with an estimate of the time required to accomplish them. We currently have 5 PhD students and 3 faculty working on the team, which provides significant but not unlimited capacity.

We describe work items below, segmented by the amount of effort required. A small effort (S) is roughly 1-5 person-days, a medium effort (M) is 6-10 person-days, and a large effort (L) is 11-20 person-days. Here, we have roughly 5 people who can each provide 5 person days per week.

- (M) Estimate quarantine capacity requirements
- (M) Estimate impact of telling high-risk individuals not to come to campus
- (L) Group testing protocol design
- (L) Segment populations into groups (enables accuracy improvements & new features)
  - (S) Estimate impact of moving from doubles to singles (requires segmenting populations into groups)
  - (S) Estimate impact of “pod” dorm structure
- (L) Simulations at the individual level (enables accuracy improvements & new features below)

- (S) Improvement to contact tracing accuracy (requires individual sims)
- (S) Improvement to risk group accuracy (requires individual sims)
- (M) Parameter estimation of number of contacts based on card swipe and network data from Cornell
- (XL) Develop and understand adaptive screening and social distancing strategies, including efforts to identify ranges of plausible parameters over which strategies should be robust.

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