**Supplementary Appendix 1. Metapopulation compartmental model**

We develop a metapopulation compartmental model that projects weekly SARS-CoV-2 cases, symptomatic cases, and daily isolations and quarantines. This model generalizes the metapopulation SEIR model in Llyod and Jansen (2004). A description of model equations is provided in Supplementary Table 1, with input parameters given in Supplementary Table 2.

In the rest of this section, we detail the initial states of the compartments and the estimation of transmission rate from the empirical data at Clemson University.

**Initial states.** In the following, compartments are considered as 6-dimensional vectors, each dimension associated with a sub-population, in the order of in-state on-campus students, out-of-state on-campus students, off-campus students, faculty, staff, and community. In addition, each compartment is indexed by , representing each of the following eight protection levels

* : unprotected (unvaccinated, no previous infection)
* : fully vaccinated w/out previous infection
* : boosted w/out previous infection
* : previously infected, unvaccinated
* : fully vaccinated w/ previous infection
* : boosted w/ previous infection

1. **Population size (Nj).** The Clemson University-affiliated population consists of active students, faculty, and staff at Clemson University between June 5, 2020 and the follow-up end date. The community population size is set to be 50000.
2. **Recovered (Rej(0)).** Initial states for university-affiliated recovered individuals at baseline consist of those who were tested positive within 90 days to the follow-up end date. The community baseline recovery rate is set at 30%.
3. **Isolation and quarantine (Qj(0), Qsj(0), Qrj(0)).** Initial states for isolation and quarantine compartments are obtained from empirical data at Clemson University, consisting of individuals who are discharged from isolation or quarantine later than the follow-up end date. Quarantined individuals are assumed to be uninfected and categorized in the Qsj(0) compartments. Qrj(0) is set to 0 across all populations. Initials for community isolation and quarantine is set to 0.
4. **Exposed, asymptomatic/symptomatic infectious (Ej(0), Aj(0), Ij(0)).** Initial states for the symptomatic infectious are obtained from empirical data. At time 0, is the number of infected individuals tested positive within the last days. The implicit assumption is that under voluntary testing, individuals get tested because they have developed symptoms. Initial states of exposed and asymptomatic infected are computed via

where , , and are the mean incubation time, mean asymptomatic infectious time, and mean symptomatic infectious time before detection/isolation, respectively (Supplementary Table 2). The initial states of symptomatic infectious in community is set to be 1% of the community population size, equally split into the six protection levels.

1. **Test positive (Tj(0), Tej(0)).** Initial states for individuals testing positive (infected, Tj(0); exposed, Tej(0)) are set to be 0 across all populations.
2. **Susceptible (Sj(0)).** Initial states for the susceptible compartments are given by

**Contact matrix and transmission rate.** Every day is divided into six time-steps, each representing four hours. On weekdays (Monday through Friday), we assume that the first time-step represents classroom time. For in-state on-campus student, out-of-state on-campus student, off-campus student, faculty, and staff subgroups, the contact matrix is given by

where is the proportion of on-campus students that are in-state, estimated using data from Clemson University. The corresponding transmission rate for the unprotected individuals is given by

The second time-step on each weekday represents work time not inside classrooms. For in-state on-campus student, out-of-state on-campus student, off-campus student, faculty, and staff subgroups, the contact matrix is given by

The corresponding transmission rate for the unprotected individuals is given by

The rest of the time-steps (third to sixth) on weekdays represent after-hours. The contact matrix is given by

The corresponding transmission rate for the unprotected individuals is given by

For weekends, the contact matrix is given by

The corresponding transmission rate for the unprotected individuals is given by

In the contact matrices, the entry represents the proportion of individuals in subgroup that have made contacts with individuals in subgroup .

**Supplementary Appendix 2. Statistical methods**

**Estimates of weekly SARS-CoV-2 cases.** Daily new cases on each day are calculated via the difference in the susceptible compartments between day *t-1* and *t.* Weekly new cases aggregates daily new infections over 7-day periods over the prediction timeframe. The number of new cases on day *t* is given by

Total number of new cases in week *w* is

**Estimates of weekly SARS-CoV-2 symptomatic infections.** Daily symptomatic cases under this framework consist of two groups of individuals, those who are detected at the beginning of the day, and those who are isolated at each time step of the day. Let be the time step in hours and be the time step in days, so that is the number of time steps per day. The number of new symptomatic cases on day *t* is

where *p* is the daily testing proportion, the sensitivity of the test for symptomatic infections, the time of symptomatic infection before isolation.

**Estimates of daily isolation and quarantine.** The number of isolations on day *t* is the total number of individuals in all isolation compartments; i.e., . The number of isolations and quarantine on day *t* is the number of individuals in all isolation/quarantine compartments; i.e., .

|  |  |
| --- | --- |
| **Compartment** | **Equation** |
| **Unprotected** |  |
| …Susceptible: |  |
| …Exposed: |  |
| …Asymptomatic infectious: |  |
| …Symptomatic infectious: |  |
| …Test positive (exposed): |  |
| …Test positive (infectious): |  |
| …Isolation: |  |
| …Quarantine (non-infected): |  |
| …Quarantine (infected): |  |
| …Recovered: |  |
| **Fully vaccinated**  **w/out previous infection** |  |
| …Susceptible: |  |
| …Exposed: |  |
| …Asymptomatic infectious: |  |
| …Symptomatic infectious: |  |
| …Test positive (exposed): |  |
| …Test positive (infectious): |  |
| …Isolation: |  |
| …Quarantine (non-infected): |  |
| …Quarantine (infected): |  |
| …Recovered: |  |
| **Boosted**  **w/out previous infection** |  |
| …Susceptible: |  |
| …Exposed: |  |
| …Asymptomatic infectious: |  |
| …Symptomatic infectious: |  |
| …Test positive (exposed): |  |
| …Test positive (infectious): |  |
| …Isolation: |  |
| …Quarantine (non-infected): |  |
| …Quarantine (infected): |  |
| …Recovered: |  |
| **Previously infected,**  **unvaccinated** |  |
| …Susceptible: |  |
| …Exposed: |  |
| …Asymptomatic infectious: |  |
| …Symptomatic infectious: |  |
| …Test positive (exposed): |  |
| …Test positive (infectious): |  |
| …Isolation: |  |
| …Quarantine (non-infected): |  |
| …Quarantine (infected): |  |
| …Recovered: |  |
| **Fully vaccinated**  **w/ previous infection** |  |
| …Susceptible: |  |
| …Exposed: |  |
| …Asymptomatic infectious: |  |
| …Symptomatic infectious: |  |
| …Test positive (exposed): |  |
| …Test positive (infectious): |  |
| …Isolation: |  |
| …Quarantine (non-infected): |  |
| …Quarantine (infected): |  |
| …Recovered: |  |
| **Boosted**  **w/ previous infection** |  |
| …Susceptible: |  |
| …Exposed: |  |
| …Asymptomatic infectious: |  |
| …Symptomatic infectious: |  |
| …Test positive (exposed): |  |
| …Test positive (infectious): |  |
| …Isolation: |  |
| …Quarantine (non-infected): |  |
| …Quarantine (infected): |  |
| …Recovered: |  |
| **If *t* is an integer, then for** | |
| Exposed: |  |
| Asymptomatic infectious: |  |
| Symptomatic infectious: |  |
| Test positive (exposed): |  |
| Test positive (infectious): |  |

**Supplementary Table 1: Equations for compartmental transmission models.** Time *t* increases from 0 to *T* days with increments of *h=Δ/24 days with Δ=4 being the increments in hours*. All compartments are 6-dimensional vectors, representing in-state on-campus students, out-of-state on-campus students, off-campus students, faculty, staff, and community numbers in this order.

\* represents the total number of infectious individuals at time step *t*. And is the vector of sub-population sizes.

|  |  |
| --- | --- |
| **Model parameter** | **Input** |
| Disease dynamics |  |
| …Mean incubation time (days): | 3 days |
| …Mean asymptomatic infectious time (days): | 10 days |
| …Mean symptomatic infection time before detection/isolation (days): | 2 days |
| …Lag between test and results: | 1 day |
| …Days in isolation: | 5 days |
| …Days in quarantine for non-infected individuals: | 5 days |
| …Days in quarantine for infected individuals: | 7.5 days |
| …Proportion of infections detected through voluntary testing: |  |
| ……On-campus students | 0.15 |
| ……Off-campus students | 0.15 |
| ……Faculty | 0.25 |
| ……Staff | 0.25 |
| ……Community | 0.20 |
| Disease reproductive number: |  |
| …On-campus students | 12.0 |
| …Off-campus students | 10.0 |
| …Faculty | 5.0 |
| …Staff | 5.5 |
| …Community | 6.0 |
| Transmission rate |  |
| …Unvaccinated: | Varies |
| …Fully vaccinated w/out previous infection: |  |
| …Boosted w/out previous infection: |  |
| …Previously infected, unvaccinated: |  |
| …Fully vaccinated w/ previous infection: |  |
| …Boosted w/ previous infection: |  |
| Contact matrix: | Varies |
| Number of close contacts per infected individual: *q* | 3 |
| Daily random surveillance tests: |  |
| …On-campus students | 1.0% |
| …Off-campus students | 1.0% |
| …Faculty | 1.0% |
| …Staff | 1.0% |
| …Community | 1.0% |
| Test sensitivity |  |
| …Exposed () | 33% |
| …Infectious () | 95% |

**Supplementary Table 2: Model input parameters, assumptions, and references.** The parameters for represent the hazard ratio of the corresponding category relative to the unvaccinated, estimated from the empirical data.