Colorado COVID-19 Mathematical Model Documentation

Prepared by the Colorado COVID-19 Modeling Group
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We use a deterministic age-structured susceptible, exposed, infected, recovered (SEIR) model to estimate the impact of interventions and behavioral changes to reduce COVID-19 transmission to date as well as to project the number of people with COVID 19 needing hospitalization, critical care and the number of deaths in Colorado under different intervention scenarios. The model has been calibrated to Colorado-specific COVID-19 metrics and demographics. Site-specific model parameters are fit to Colorado COVID-19 hospitalization data, and time-varying parameters are updated weekly. The model can be used to project the number of hospitalizations, ICU need, and deaths in the coming months, under different intervention scenarios, including changing levels of social distancing, mask wearing, and introduction of contact tracing. This documentation describes the model, data sets used, and key assumptions and their bases.

Key model updates

The model has been updated based on the latest available data on Colorado hospitalizations for COVID-19 and to streamline the model-fitting process.

- The model is now being fit to estimate reductions in the contact rate ("social distancing") for each two-week period since the outbreak began. Previously the cut-points were estimated for time intervals defined based on implementation of policy measures (e.g., for the Stay at home period), and then for one-week periods starting with the "Safer-at-home" initiative. We have made this shift to decrease both the number of parameters being estimated and assumptions about the time period over which social distancing has changed. This change will also decrease week-to-week variation in the estimates of contact reduction/Re.
- The length of hospital and ICU stay for COVID-19 patients has been updated to reflect current data from Colorado hospitals on the mean length of stay among COVID-19 ICU patients and those that were hospitalized but did not require critical care.
- Using updated length of stay data, the proportion of symptomatic individuals who are hospitalized (both in the ICU and non-ICU hospitalizations) has been updated using model-fitting techniques.
- Mortality rates attributed to COVID-19 of hospitalized patients (both in the ICU and non-ICU hospitalizations) has been updated based on the most current available data specific to Colorado.

Model structure

In the model exposed individuals incubate infections for 4.2 days before becoming infectious. This is based on evidence that the incubation period for SARS-CoV-2 (the time between infection and symptom onset) is approximately 5.2 days [1-3], and that individuals are infectious before symptom onset [4-7]. Presymptomatic infectiousness is currently thought to be greatest in the day before symptom onset [8] and thus we assume 1 day of presymptomatic infectiousness among individuals who become symptomatic. Infected individuals can be either symptomatic or asymptomatic. The infectious period is the same regardless of symptoms and lasts for 9 days [6, 8]. Both the latent period and infectious period are exponentially distributed in the model. The model accounts for evidence that asymptomatic individuals are probably less infectious than symptomatic individuals [9], including includes a ratio of transmission probability for symptomatic vs. asymptomatic individuals which is estimated via model fitting (described below).

We developed an age-structured model with four separate age compartments (0-19, 20-39, 40-64, and 65+) based on evidence that the probability an infected individual develops symptoms [10] and the probability a symptomatic individual is hospitalized [11-13] are age-dependent. We used Colorado demographic data for 2016 from the US Census to define age and population structure and adjusted for a 9% relative population increase since 2016 based on current estimates of population growth in the area. We estimated age-dependent probabilities that an infected individual is symptomatic, estimating the product of the age distribution of Colorado within each age-compartment and the age-group-specific symptomatic fraction as shown in Table 1 ([10], personal communication). We used Colorado COVID-19 hospitalization and intensive care unit (ICU) data to estimate the probability of hospitalization and ICU need for each age group using model fitting techniques (Table 1). Symptomatic cases that require hospital care are moved into either a non-ICU hospitalized, or ICU compartment 8 days after the onset of symptoms [3]. We assume that the average length of hospital stay is dependent on both age and whether or not critical care is required. These values are based on hospital data for COVID-19 patients in Colorado through mid-August (Table 2). Data on length of stay by age and month are shown in Appendix Table 1. In the model, no further transmission occurs once the patient enters the hospital.

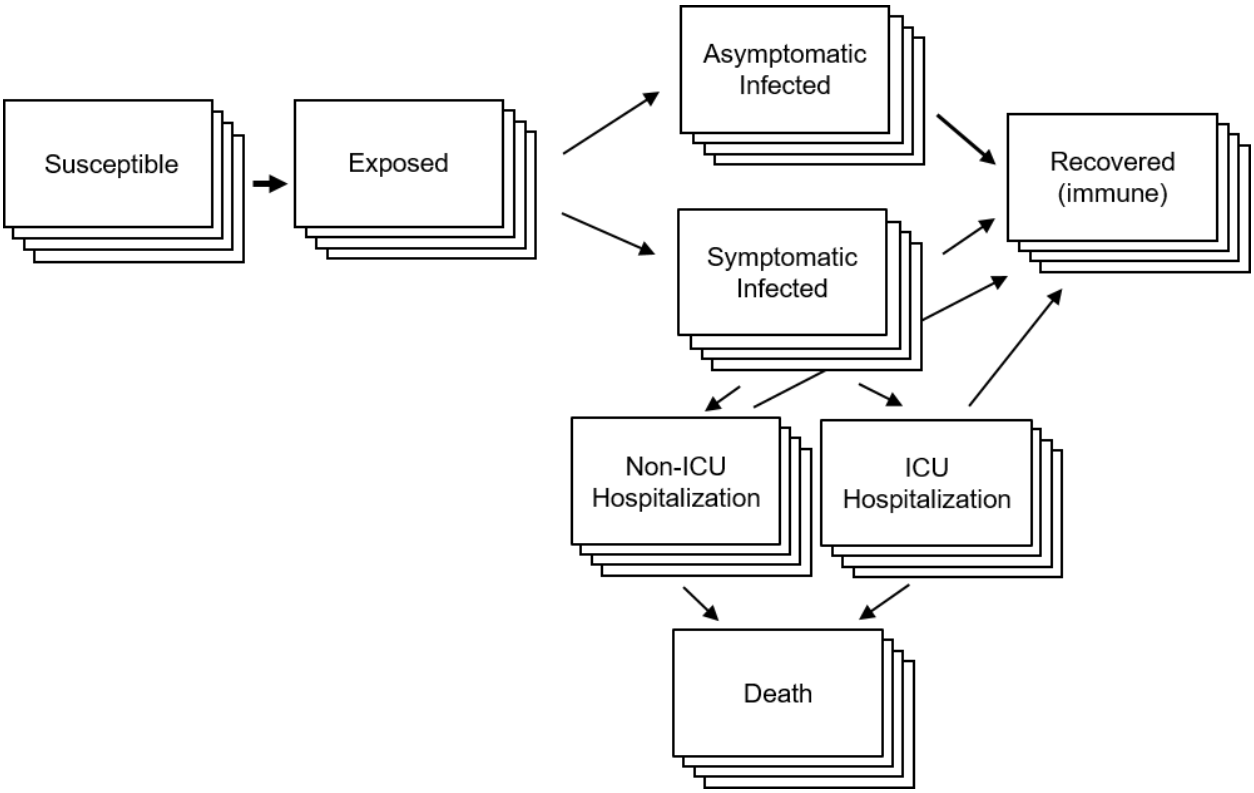

Figure 1. The base structure of the SEIR model. The model is age-stratified, with separate compartments for each of four age groups 0-19, 20-39, 40-64, and 65+. The symptomatic infected compartment includes a 1-day period where individuals are infectious but not yet symptomatic.

Table 1. Probabilities of symptoms, hospitalization and critical care need by age group. The probabilities of hospitalization are Colorado-specific estimates, derived from fitting age-specific hospitalization curves from the model to COVID-19 hospitalization data with onset date on or before March 27. COVID-19 hospitalization data sources and model fitting methods are described, below.

Age Category	**Proportion of infected individuals that develop symptoms from [10]**	**Probability of non-ICU hospitalization given symptomatic**	**Probability of needing ICU given symptomatic**
0-19	0.11	0.0164	0.00396
20-39	0.36	0.0291	0.00752
40-64	0.56	0.0433	0.0182
65+	0.77	0.0724	0.0304

Table 2. Length of stay and mortality by age category and ICU vs non-ICU hospitalization from Colorado-specific COVID-19 hospitalizations based Colorado COVID-19 patients hospitalized through August 2020, and COVID-19 case reports through August 11 provided by CDPHE.

Age Category	Mean length of non-ICU hospitalization (days)*	Mean length of ICU stay (days)	Probability of death among hospitalized patients that don't need ICU care	Probability of death among hospitalized patients requiring ICU-care	Probability of death among non-hospitalized reported cases**
0-19	4.05	6.35	0.0000	0.0571	0.00008
20-39	5.49	9.91	0.0000	0.0615	0.00014
40-64	7.36	13.47	0.0086	0.1674	0.00127
65+	10.02	10.82	0.1449	0.3920	0.03389

*Mean length of ICU stay is the mean time a COVID-19 ICU patient spends in the ICU. As ICU patients spend some time in the non-ICU as well, we account for this as follows. Non-ICU length of stay was calculated as non-ICU patient's length of stay plus the difference between total length of stay and ICU length of stay for ICU patients, multiplied by the proportion of hospitalized patients that enter the ICU.

** Using CDPHE COVID-19 data as of August 11, non-hospitalized mortality was calculated as the proportion of all non-hospitalized cases with symptom onset date on or before June 8 who died, by age strata, then adjusted for assumed case detection rate at the time of death.

Mortality is based on the probability of death based on age and hospitalization status (ICU, hospitalized without ICU care, not hospitalized) (Table 2) and ICU capacity. We estimated probability of death for hospitalized COVID-19 patients based on hospital data for COVID-19 patients in Colorado through mid-June. Mortality among non-hospitalized COVID-19 cases was calculated as the proportion of all non-hospitalized cases with onset date on or before June 8th who died, by age, then adjusted for assumed case detection rate at the time of death, using reported COVID-19 case data in Colorado through August 11. We estimate additional mortality will occur if hospital capacity is reached. We assume that once available ICU beds are full, all cases requiring ICU in excess of availability will die. ICU bed capacity is set at 1,800 beds. Recent estimates of ICU use when elective surgeries are cancelled indicate that approximately 1,800 ICU beds would be available for COVID 19 patients, noting that hospitals may increase surge capacity in coming months.

Recovered individuals are assumed to remain immune to infection. We assume random population mixing, and that infection probability does not vary by age or sex. The model assumes a single introduction event occurring on January 24, which we extrapolated from the first reported cases in Colorado and estimates of under-reporting in early stages of the outbreak. There are no additional importations, migration, or non-COVID-19 related deaths in the system.

Interventions included in the model

The model includes four interventions that have been implemented in Colorado to slow the spread of infections: 1) social distancing; 2) mask wearing; 3) case isolation and 4) contact tracing.

Social distancing. Social distancing measures were adopted in Colorado starting in mid-March to reduce person-to-person contacts and slow the spread of infection. We model social distancing using a parameter that describes the percent decrease in effective contacts between susceptible and infectious individuals. This parameter accounts for social distancing policies intended to avoid

contact altogether (e.g., through workplace and school closures) as well as policies and individual behaviors to reduce potential contact with the virus (e.g., maintaining at least 6 feet of distance between people outside of one's household, and handwashing). To account for the changes in the degree of social distancing over time in relation to policy measures, we define and fit a social distancing parameter for each 14-day period from the start of the epidemic. We note that we fit our model weekly, which means that the most recent social distancing parameter will represent a 7-day period in on week and a 14-day period the following week.

Mask wearing. As of April 4, Coloradoans had been advised to wear masks at work and in public. Masks can trap viral particles shed by infectious individuals and prevent their transmission to others. We model the effectiveness of mask wearing as a reduction in transmission by asymptomatic and presymptomatic individuals based on current evidence [14, 15]. The effectiveness of mask wearing depends on both the ability of the mask to trap viral particles and the proportion of the population wearing masks appropriately. We assume cloth face masks are approximately 50% effective at trapping viral particles shed by infectious individuals [14, 15], cautioning that there remains considerable uncertainty about this assumption. We also assume that masks impact the transmission risk for contacts outside of the household. Prior studies have estimated that approximate 23% of a person's respiratory-virus relevant contacts occur at home [16]. In light of evidence that people are spending more time at home during the COVID-19 pandemic, we assume that 33% of an individual's contacts are with household members - mask wearing outside the home is assumed to impact the approximately 67% of total contacts that are outside the home. Recognizing that some transmission may also be occurring via fomites (including via touching masks), we use the aforementioned assumptions to model the effectiveness of masks as a 30.2% reduction in infectiousness by asymptomatic individuals that wear masks. Additionally, we assume mask wearing reduces presymptomatic transmission by infected individuals who will ultimately become symptomatic. This is modeled as a net 3.77% reduction in infectiousness among symptomatic individuals that wear masks, assuming an individual who ultimately becomes symptomatic is infectious for 9 days and asymptomatic for the first day. Our model does not account for potential reduction in infectiousness by symptomatic individuals by wearing masks, as most are assumed to be isolated, but we note that this would result in an additional benefit of mask wearing [17]. We assume 50% of the population began wearing masks in public beginning on 4/4, borrowing the assumptions of [14], coinciding with the Governor's press conference advising Coloradoans to wear masks. We assume the proportion of people wearing masks is 70% starting April 27, the date that mask wearing became mandatory in public spaces in the Denver metro region, based on recent survey data indicating high levels of mask wearing in Colorado [18]. We assume mask wearing increased to 90% on July 16th, coinciding with a state-wide mask order.

Symptomatic Case isolation. Since the beginning of the pandemic, individuals with symptoms consistent with COVID-19 have been encouraged to stay home and self-isolate in order to prevent the spread of infections. The effectiveness of this strategy depends both on the time between the onset of infectiousness and containment, as well as the percent of symptomatic cases contained, and the ability to isolate from household contacts. We assume case isolation reduces transmission by symptomatic individuals to non-household contacts only (estimated to be 67% of total contacts) during the symptomatic, infectious period (8 of 9 infectious days). Case isolation is assumed to begin on March 5, the date the first COVID-19 cases were reported in Colorado. We note that the

population of symptomatic cases contained may include people who have symptoms but have not tested positive. Our estimate of the proportion of cases that self-isolate is based on model fitting.

Contact tracing. Contact tracing has been proposed as a key strategy for controlling the spread of COVID-19 and is being implemented progressively throughout Colorado. We include contact tracing in the model to project the potential impact of contact tracing on COVID-19 in Colorado based on the methods of others [19, 20]. We point out that numerous assumptions need to be made on key model parameters, absent Colorado-specific data at this time. Contact tracing is only included in model projections.

Contact tracing is incorporated in the model through inclusion of an additional compartment in each age category, the Isolated Infectious compartment (II), as per [20]. Individuals who move to the isolated infectious compartment are exposed and infectious individuals who have been identified by public health officials, are told to quarantine, and comply. Infectious individuals are removed from both the I (symptomatic) and A (asymptomatic) compartments to the II compartment at the following rate: $pID*pCT*\kappa*\pi*\omega$. These parameters are as follows:

- pID is the proportion of total infections, including asymptomatic and symptomatic, that are detected by public health authorities (see Estimating the proportion of cases detected, below).
- pCT is the proportion of detected cases traced. This value is dependent on contact-tracing capacity and the current infection rate. With a current detection rate of ~250 symptomatic cases/day and current theoretical contact tracing capacity of 165 cases/day, this is currently estimated at 0.66. However, as there is limited data on the true current contact tracing capacity throughout the state of Colorado, we allow this figure to vary from 0.2 to 0.8 to demonstrate the impact of increasing tracing capacity. This figure will be updated in the future as data on capacity becomes available. Unless stated otherwise, we assume pCT = 0.4 for all other contact tracing projections.
- κ is the average number of contacts per identified infectious individual. This value varies based on the definition of a contact, as well as the level of social distancing in a society. Current estimates from contact tracing vary from 20 (South Korea) to 3.5 (San Francisco) based on conversations with representatives of these programs. This number is dampened by the proportion of individuals successfully traced (estimates from San Francisco = ~70%), as well as the proportion of contacts who comply with quarantine. For the purpose of the current model, we examine the average number of contacts who are successfully traced as well as comply with quarantine, values ranging from 1 to 5. When not explicitly varying the number of contacts, we hold the value constant at 3.
- π is the probability that a traced infectious contact is isolated before infecting other susceptible individuals. This value is dependent on the lag between symptom onset and case report to health authorities, as well as the amount of time it takes for contact tracing to occur after a case is reported. In Colorado, we typically see a lag of approximately 7 days between symptom onset and case report – which translates to an average of 8 days between the onset of infectiousness and report. Assuming contacts are reached within the targeted 24 hours of case report, for any infectious contacts that occurred in the 9 days of case infectiousness, on average 5/9 of those days could have led to an infectious contact that could have infected another individual in those 5 days between onset of infectiousness and tracing. Likewise, with a 48-hour lag between report and contact, on average 6/10 of the

case-infectious days could have led to an infectious contact that could have infected another individual. We model π for 24, 48, and 72-hour lags in contact tracing, and assume an average of 48 hours for all contact tracing models when not explicitly stated otherwise.

- ω is the probability a contact-traced individual is infected and has been estimated from the literature [6, 21-25]. Estimates for secondary attack rates among household contacts range from 4.6% to 19.3%, and among non-household contacts range from 0% to 0.55%. We use the approximate average 9% secondary attack rate among household contacts and 0.275% attack rate among non-household contacts. We assume the average individual has two household contacts, and, if those are the most likely individuals to be successfully traced. Thus, if only 2 contacts are traced per case, both are likely to be household, and we use the household secondary attack rate of 9%, however, if 4 contacts are traced, half are assumed to be non-household contacts, and we assume the secondary attack rate is the average of the household and non-household rate at 4.6%. When not explicitly varying the number of contacts successfully traced, we hold the value of κ constant at 3, with the assumption of 2 household contacts and one non-household contact ω is estimated at 6.1%.

Parameter estimation

We use model fitting methods to estimate the parameter values which may vary regionally and/or for which there is considerable uncertainty in the current literature. The model-fitting process involves comparing model outputs to observed COVID-19 hospitalization data in Colorado in order to align estimates.

Hospitalization data. We use hospitalization data to fit our model as this is seen as a more stable indicator of COVID-19 transmission and is not sensitive to changes in testing capacity. The total hospitalizations (ICU + non-ICU) as predicted by the model are compared to Colorado COVID-19 hospitalization data provided by CDPHE and the EMResource hospital census of hospitalizations. For model fitting, we use reported COVID hospitalizations with hospital admission dates through April 7 provided by CDPHE and the EMResource hospital census of hospitalizations starting 04/08 because the EMResource hospital census appeared to undercount COVID-19 hospitalizations before that date. Because the EMResource provides an aggregate count of all hospitalized patient, we additionally used CDPHE resource utilization data ("COPHS") which provides counts of hospitalized patients by age group to estimate age-specific hospitalization rates, as described below.

Model fitting. Best-fitting parameter values were identified via a least squares cost function minimizing the comparison between the estimated proportion of expected cases that would be detected in the model and the number of confirmed COVID-19 cases in Colorado (Figure 1). The cost function was minimized using a two-stage fitting algorithm in R, first applying a pseudo-random optimization algorithm [26] to find a region of minimum difference between the model and the data. The second phase used least squares optimization applying the Levenberg-Marquardt algorithm [27].

In order to fit the model to hospitalizations early in the epidemic, the rate of infection (beta), proportion of symptomatic individuals that self-isolated after March 5 (siI), and the proportionate increase in transmission comparing symptomatic to asymptomatic infections (lambda) were fit using data on hospitalizations up to March 27. Priors for hospitalization rates came from [11]. Given the parameter values for Beta and lambda, we estimated age-specific hospitalization and ICU

rates, fitting the curves to the initial phase of the epidemic for CDPHE COPHS data with onset date on or before March 27. These estimates were aligned to the age groupings in the model: 0-19, 20-39, 40-64, and 65+.

Estimating the course of COVID-19 transmission to date

Estimating social distancing to date. Model fitting using the same algorithms described above is used to estimate the level of social distancing (measured as a percent decrease in effective contacts)biweekly in Colorado, beginning at March 1st, the first recorded COVID-19 hospitalization in Colorado, and up to the current date. To allow for weekly updates of the current state of the epidemic in Colorado, each week we fit a parameter to the previous two weeks of data weekly, as well as refit the previous two bi-weekly periods to capture the changing trends in the data.

Estimating proportion of infections detected. We estimate the proportion of SARS-COV2 infections (including both asymptomatic and symptomatic infections) that are being captured by Colorado state surveillance systems over time based using the SEIR model outputs of the daily number of new infections (symptomatic + asymptomatic). We compared this output to the number of cases captured by state surveillance systems. We used the number of cases reported by CDPHE, using the onset date of symptoms or, if this is not available, the date of report minus 7 days based on typical lags for the infection. The ratio of reported cases to model output gives us the estimated proportion of infections detected.

Estimation of the effective reproductive number. To compute the effective reproductive number (Re) for the age-structured model, we followed two separate processes. The first follows the process outlined in [28]. The Colorado model includes 4 age categories as well as subcompartments for exposed, asymptomatic, and symptomatic individuals. We consider all 12 compartments which contain infected individuals and collect them in a vector. Roughly speaking, the matrix that updates the population numbers in the vector is called the Next Generation Matrix. The dominant eigenvalue for this matrix is Re, which we thus compute at each timepoint. We additionally estimated Re from the model output alone (as opposed to using parameter values, as with the former method), giving a partially smoothed estimate akin to the methods of [29]. To estimate Re from model output we calculated an approximate (4-day average) estimate of individuals newly exposed on a given day and divided by the number of infectious individuals four-days prior, divided by the length of the infectious period (equation below).

$$\frac{\frac{E(t)}{4}}{\frac{I(t-4)}{9}}$$

Current parameter estimates and estimates of the reproductive number are described separately: see Parameter estimates and model fit.

Because we base our parameter estimates on COVID-19 hospitalization data, our estimates of the current state of COVID-19 in Colorado reflect the state of infections occurring approximately 2 weeks prior. This because there is an approximately 13-day lag, on average, between infection and hospitalization. Hospitalization data is a robust indicator of transmission trends, as reported COVID-19 case data are sensitive to testing capacity and consequently may represent a variable

proportion of actual infections over time when testing capacity is changing, however it is important to recognize that hospitalizations today reflect infections generally occurring two weeks ago.

The model is updated approximately weekly with to re-estimate time-varying parameters including social distancing and the proportion of infections detected.

Projecting the future course of COVID-19 in Colorado

The SEIR model, using the most recent parameter estimates, are used to drive the model and generate projections of the estimated number of cases, hospital needs and deaths in the future. Model projections are generated based on scenarios – or "what ifs." For example, projections can be generated to evaluate the estimate number of hospitalizations if social distancing is relaxed or contact tracing is pursued. We assume a start date of these interventions of 13 days before the last model fit, accounting for the lag between infections and hospitalizations.

The Shiny App allows generation of projections varying the four key interventions available to control COVID-19. This includes

- ***Social distancing.*** In model projections, the degree of social distancing can be varied at different points and time and for different age groups. For example, one can evaluate changing social distancing in two phases: 1) the present through mid-August and 2) from mid-August forward, corresponding with the start of school. Given CDC recommendations that older adults adopt extra precautions to avoid getting COVID-19, projections can be generated assuming a proportion of older adults adopt high levels of social distancing (80%). The remainder are assumed to adopt the same social distancing levels as the general public.
- ***Mask wearing.*** The percent of the population wearing masks can be varied.
- ***Case isolation.*** In model projections, projections can be generated to evaluate the potential impact of increased case isolation due to increased testing capacity (assuming those who test positive are more likely to self-isolate). This is modeled as an increase in case detection and isolation of 5% per week, to a maximum of 80% of all symptomatic cases self-isolating.
- ***Contact tracing.*** Contact tracing can be modeled varying the number of contacts traced per identified case and the average time lag between case identification and the containment of contacts.

Caveats and limitations. While our model of SARS-CoV-2 is based on current scientific literature, the science is evolving rapidly, and our understanding of this virus is incomplete. The current model does not account for any seasonal variation in the infectiousness of SARS-CoV-2 and the associated illness of COVID-19. There is evidence to suggest that seasonal changes typically associated with the summer season in temperate climate regions (rising temperature and humidity) may reduce SARS-CoV-2 transmission. Several recent studies assessing the impacts of temperature and/or humidity on COVID-19 transmission have suggested that low temperatures and low humidity are the most favorable conditions for transmission, with a general decreasing trend in infections found to be associated with rising temperature, humidity or both [30-35]. This is consistent with other studies of temperature and humidity trends and the winter-dominant seasonal pattern that has been previously identified for influenza strains [36-38] as well as other closely related beta-coronaviruses [39-41]. The magnitude of any seasonal impact is not well characterized but if present, may slow transmission in the summer months and accelerate

transmission in the winter months. Additionally, our understanding of immunity to SARS-CoV-2 is incomplete and we do not yet fully understand how long an individual is immune to the virus following infection or how immunity varies among previously infected populations.

The current model also does not account for potential changes in hospital capacity due to influenza. In severe influenza years, patients hospitalized with influenza can comprise a substantial proportion of ICU beds. We are developing scenarios that estimate hospital and ICU capacity in severe and mild influenza years which can be used to better estimate hospital capacity in the winter months.

The model assumes random mixing in the population, a common assumption in transmission models, however, in reality, people do not mix randomly, and non-random mixing may lead to high-risk subpopulations that are not well characterized in this model [42, 43].

Code

Code for our models is posted on Github: https://github.com/agb85/covid-19

Appendix

The length of time a COVID-19 patient spends in the hospital varies by age, as seen in the Colorado hospital data, below. The length of stay for COVID-19 patients that do not require ICU care has remained relatively constant over time. Length of ICU stay and total hospital length of stay appears to have modestly declined for adult age groups. We caution there is considerable variability in the length of stay by patient as evidenced by the high standard deviations. We continue to closely monitor these data and evaluate trends.

Table 1. Mean length of stay of Colorado COVID-19 patients for ICU and non-ICU hospitalizations by age and month based on data provided by Colorado hospitals for patients admitted on or before June 30, 2020 with surveillance through mid-August.

Month of Admission	Ages 0 – 19, mean (SD)	Ages 20 – 39, mean (SD)	Ages 40 – 64, mean (SD)	Ages 65+, mean (SD)
ICU Patients (all days)*				
March	8.0 (5.6)	15.4 (11.8)	21.1 (15.3)	18.8 (14.2)
April	9.1 (9.8)	17.4 (17.2)	21.0 (17.1)	17.3 (15.5)
May	6.0 (7.1)	12.9 (15.3)	18.3 (15.7)	15.9 (15.2)
June	14.6 (15.3)	11.3 (11.7)	14.7 (11.9)	14.8 (12.4)
ICU Patients (ICU days)*				
March	6.3	9.8	13.9	11.6
April	6.8	11.5	14.8	10.9
May	3.7	8.1	11.9	10.1
June	13.4	6.9	10.1	10.1
Non- ICU Hospitalization				
March	1.4 (0.5)	3.4 (2.1)	4.6 (4.9)	7.0 (7.9)
April	3.2 (3.7)	3.8 (3.2)	4.6 (4.8)	8.0 (7.1)
May	4.0 (4.9)	3.7 (3.0)	4.8 (3.8)	6.0 (5.6)
June	3.5 (4.7)	3.0 (2.0)	5.1 (5.7)	6.6 (5.7)

*Includes days spent in the ICU and days spent in non-ICU care in the hospital.

*Standard deviation was not available for this measure.

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