Colorado COVID-19 Regional 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 current state of SARS-CoV-2 transmission in regions within Colorado. The model has been calibrated to regional-specific COVID-19 metrics and demographics. Site-specific model parameters are fit to either COVID-19 hospitalization data or case reports, and time-varying parameters estimating current levels of transmission control are updated regularly. This documentation describes the models, data sets used, and key assumptions.

Definition of Regions

The regions used in our models were selected based on three criteria:1) the need for sufficiently large populations within a region to allow for model-based estimation; 2) groupings consistent with how Coloradans mix with each other; and 3) groupings that are consistent with public-health jurisdictions. While the county is a desirable unit of analysis for local public health agencies, many counties in Colorado have populations that are too small to allow stable estimation. Moreover, in many parts of the state, populations regularly mix across county boundaries. Prior work by our team identified 26 distinct mixing regions within Colorado using cell-phone based mobility data (Figure 1 and [1]). SARS-CoV-2, like most infectious diseases, is not evenly distributed across geographic regions, but rather, it clusters within highly connected populations. This leads to spatial variability in infections – one area may be an infection hotspot, another may have few infections, and the location of hotspots may vary over time. For this reason, we used these mixing regions to inform the units of analysis for the regional models.

The regional models use geographic regions for analysis, either selected counties or LPHA regions. The LPHA regions are based on local public health agency coalitions. There are 11 LPHA regions in Colorado: Central, Central Mountains, East Central, Metro, Northeast, Northwest, San Luis Valley, South Central, Southeast, Southwest, and the West Central Partnership (Table 1 and Figure 1). County-level models have been created for selected counties, including El Paso and the counties within the Metro LPHA region. Within the Metro LPHA region, there is sufficient population to allow generation of county-level estimates for seven of the nine counties which is generally consistent with mixing patterns. Clear Creek and Gilpin counties have small populations (9,379 and 5,924 residents, respectively) which prevented us from generating independent estimates for these counties. Instead, Jefferson, Clear Creek and Gilpin counties are combined into a single unit for estimation (we refer to this unit as "Jefferson plus"), due to the considerable mixing across these counties. We note that Jefferson County comprises 97% of the population in these three counties.

There are two notable caveats. First, the distribution of infections may not be uniform within each region. For example, infection prevalence may be higher in one area and lower in other parts of the region. But assuming there is population mixing within the region, high levels of infection in one area can to spread throughout the region. Second, populations move across regions and this can lead to spread of infections between units. For example, the flow of populations from the Metro LPHA region to the Central Mountains LPHA region can lead to import and export of virus between these regions. Future iterations of the model will examine the importance mixing across regions.

Table 1. Description of the regions used in this report, including the 11 LPHA Regions and eight selected counties. Population estimates are based on 2020 US Census Projections provided by the Colorado Demography Office.

|	Counties (most populous in bold)	Population*
LPHA Region		
Central	Chaffee, **El Paso**, Lake, Park, Teller	810,420
Central Mountains	Eagle, **Garfield**, Grand, Pitkin, Summit	182,689
East Central	Cheyenne, **Elbert**, Kit Carson, Lincoln	43,032
Metro	Adams, Arapahoe, Boulder, Broomfield, Clear Creek, **Denver**, Douglas, Gilpin, Jefferson	3,291,794
Northeast	**Larimer**, Logan, Morgan, Phillips, Sedgwick, Washington, Weld, Yuma	765,265
Northwest	Jackson, **Mesa**, Moffat, Rio Blanco, Routt	203,301
San Luis Valley	**Alamosa**, Conejos, Costilla, Rio Grande, Saguache	46,472
South Central	Custer, Fremont, Huerfano, Las Animas, **Pueblo**	243,196
Southeast	Baca, Bent, Crowley, Kiowa, **Otero**, Prowers	46,938
Southwest	Archuleta, Dolores, **La Plata**, Montezuma, San Juan	102,154
West Central Partnership	Delta, Gunnison, Hinsdale, Mineral, **Montrose**, Ouray, San Miguel	106,839
Selected Counties		
Adams	Adams	528,857
Arapahoe	Arapahoe	664,988
Boulder	Boulder	330,978
Broomfield	Broomfield	72,827
Denver	Denver	737,854
Douglas	Douglas	354,331
Jefferson plus*	Clear Creek, Gilpin, Jefferson	601,959
El Paso	El Paso	737,354

*The Jefferson plus group includes Jefferson (population 586,656), Clear Creek (population 9,379) and Gilpin (population 5,924).
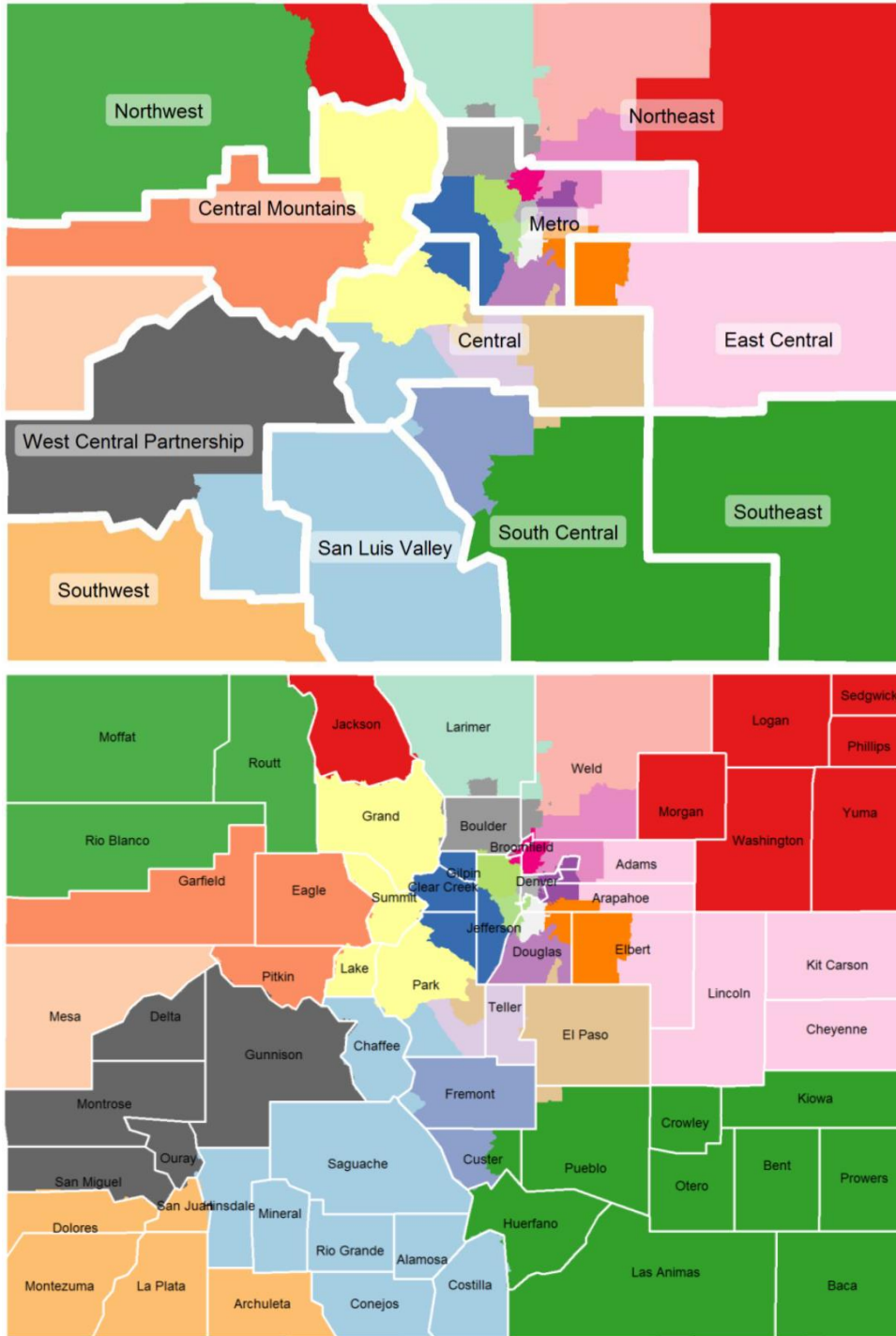
Figure 1. Mobility communities (color fill) and alignment with the 11 LPHA regions (top panel) and Colorado counties (bottom panel). The 26 mobility communities are defined using mobile phone data and described in [Adams et al 2020](#).

Model structure

A deterministic age-structured susceptible-exposed-infectious-recovered (SEIR) model is generated for each region. The base model structure is identical to the state-wide model and shown in Figure 2 (the state-wide model is described here). The key difference is that a model is the baseline transmission parameter, β, is allowed to vary by region. Additionally, mortality is not included in the regional models as this is not required for the metrics we are estimating.
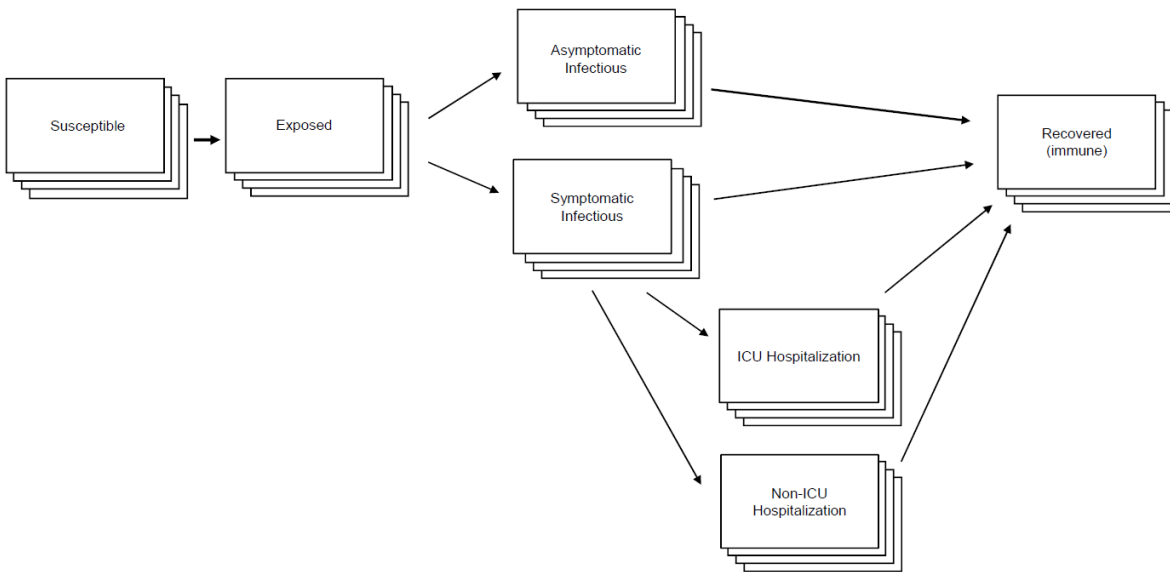
Figure 2. The base structure of the SEIR model. The model is age-stratified, with separate compartments for each of four age groups 0-19, 20-39, 40-64, and 65+. The symptomatic infected compartment includes a 1-day period where individuals are infectious but not yet symptomatic.

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 [2-4], and that individuals are infectious before symptom onset [5-8]. Presymptomatic infectiousness is currently thought to be greatest in the day before symptom onset [9] 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 [7, 9]. Both the latent period and infectious period are exponentially distributed in the model. In light of evidence that asymptomatic individuals are probably less infectious than symptomatic individuals [10], a ratio of the transmission probability for symptomatic vs. asymptomatic individuals is included in the model, λ. We use the same value of λ as used in the state-level model (λ was estimated using model-fitting approaches).

The model is age-structured model with four separate age compartments (0-19, 20-39, 40-64, and 65+) in light of evidence that the probability an infected individual develops symptoms [11] and the probability a symptomatic individual is hospitalized [12-14] are age-dependent. The population in each age category in each region is based on age- and region-specific demographic data provided by the Colorado Demography Office (Appendix Table A1).

In the model, infected individual can be symptomatic or asymptomatic, and a fraction of the symptomatic individuals require hospital care. Symptomatic cases that require hospital care are moved into either a non-ICU hospitalized, or ICU compartment 8 days after the onset of symptoms [4]. The probability an infected individual develops symptoms, the probability that a symptomatic individual requires hospital care (non-acute or intensive care), and the length of stay in the hospital are age-dependent and the same as those used in the state-level model. Briefly, the probability that an individual is symptomatic is drawn from the literature and weighted to the Colorado age-distribution ([11], personal communication). The probability of requiring hospital care and the length of stay is based on Colorado hospitalization data and these probabilities change over time due to improvements in care for COVID-19 patients. In the model, no further transmission occurs once the patient enters the hospital.

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.

Parameter estimation

We use model-fitting methods to estimate two key parameters.

The first parameter, β, is **the rate of infection**, a measure of the rate at which infections spread from infected to susceptible individuals in the absence of control. It depends both on the contact rate – the rate at which infected and susceptible indivdiuals interact – and the probability that if there is an interaction, the susceptible individual becomes infected. Because the frequency and types of contacts can vary regionally, we allow β to vary by region. This implies that, in the absence of any control measures, SARS-CoV-2 will spread more rapidly in areas where β is greater, and more slowly in areas where β is lower. Within each region, β is constant over time.

The second parameter, the **transmission control (TC)** parameter, is a measure of the reductions in transmission-relevant contacts as a result of policy and individual-level behavioral changes compared to a situation with transmission uncontrolled, as in the very early days of the pandemic. TC is defined for each region and varies over time. TC at any time point incorporates the collective impact of measures such as mask wearing, contact tracing, isolation of cases, social distancing, closure of businesses, working from home, improved ventilation and moving activities outside. Technically, TC describes the percent reduction in effective contacts between infected and susceptible individuals and is incorporated in the model in the equation: β(1 – TC). TC is estimated for each region and, within each region, for each two-week period since the outbreak began.

The model-fitting process involves comparing model outputs to observed COVID-19 case and/or hospitalization data in Colorado in order to optimize model fit and infer parameter values.

Hospitalization data. When possible, we use COVID-19 hospitalization data for parameter estimation as COVID-19 hospitalizations provide a stable indicator of SARS-CoV-2 transmission and they are sensitive to changes in testing capacity. Region-specific daily COVID hospitalizations are ascertained using data from COvid Patient Hospitalization Surveillance (COPHS), provided by CDPHE. Patients are assigned to regions based on their home zip codes. These data are used to

generate a daily census of COVID-19 hospitalized patients by region. We note that by assigning patients to regions based on their home residence, rather than the hospital location, these hospitalizations reflect areas where people are likely being exposed to the virus but may not reflect regional hospital demand as patients may seek care or be transferred across regional boundaries.

Case data. In regions where population sizes are small, few COVID-19 hospitalizations may occur, necessitating the use of additional information to assess SARS-CoV-2 transmission. Reported cases provide an additional indicator of SARS-CoV-2 transmission but reported cases are sensitive to testing capacity and thus represent a variable proportion of true infections over the course of the epidemic (Figure 3). Using the state-level model, we estimate the proportion of infections detected by comparing the model-estimated daily number of new infections to the daily number of reported infections. The proportion of infections detected was estimated to be low at the beginning of the epidemic (<20%). Starting in June, the estimated proportion of infections detected jumped with a massive increase in testing and have remained relatively steady at ~40%.

Region-specific daily SARS-CoV-2 reported infections are ascertained using the CEDRS database provided by CDPHE. This database includes all reported cases of SARS-CoV-2 in Colorado. Cases are assigned to regions based on their home zipcode and to date by symptom onset date. If onset date is missing, the onset date imputed by CDPHE is used. The 7-day average proportion of infections detected, estimated from the state-level model, is then used to scale reported case data for model fitting, allowing comparison of model-estimated infections to the reported case data.

Model fitting. Best-fitting parameter values were identified via a least squares cost function minimizing the comparison between the estimated proportion of expected hospitalizations or cases that would be detected in the model and the number of confirmed COVID-19 hospitalizations or cases in Colorado. The cost function was minimized using a two-stage fitting algorithm in R, first applying a pseudo-random optimization algorithm [15] 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 [16].

Model fitting was first used to estimate the rate of infection, β, separately for each region. β was estimated by fitting model estimated hospitalizations (ICU + non-ICU) to observed regional hospitalizations during early part of the epidemic, while exponential growth was occurring, and before implementation of a state-wide stay at home order on March 27th. In the 4 regions with small population sizes and few hospitalizations (San Luis Valley, Southeast, Southwest, and West Central Partnership), β was estimated by fitting model estimated infections to reported hospitalizations and cases, adjusted for the proportion of infections detected as described above. Estimates of β by region are provided in Table A2.

The same model fitting approaches were then used to estimate the level of transmission control TC, for each region and, within each region, for each two-week period since March 1st, the date of the first recorded COVID-19 hospitalization in Colorado. As above, hospitalization data were used for model fitting in most regions, and hospitalization and case data were used for the four listed previously. Each time the model is updated, TC is re-estimated for the most recent three periods. Due to the lag between exposure and hospitalization (estimated at approximately 13 days), the most recent estimates of transmission control reflect the level of contact rates approximately two weeks prior to the date estimated.

COVID-19 Infections: Daily New Infections Reported to CDPHE vs. Daily New Infections (Symptomatic + Asymptomatic) Estimated by Model, Colorado 2020
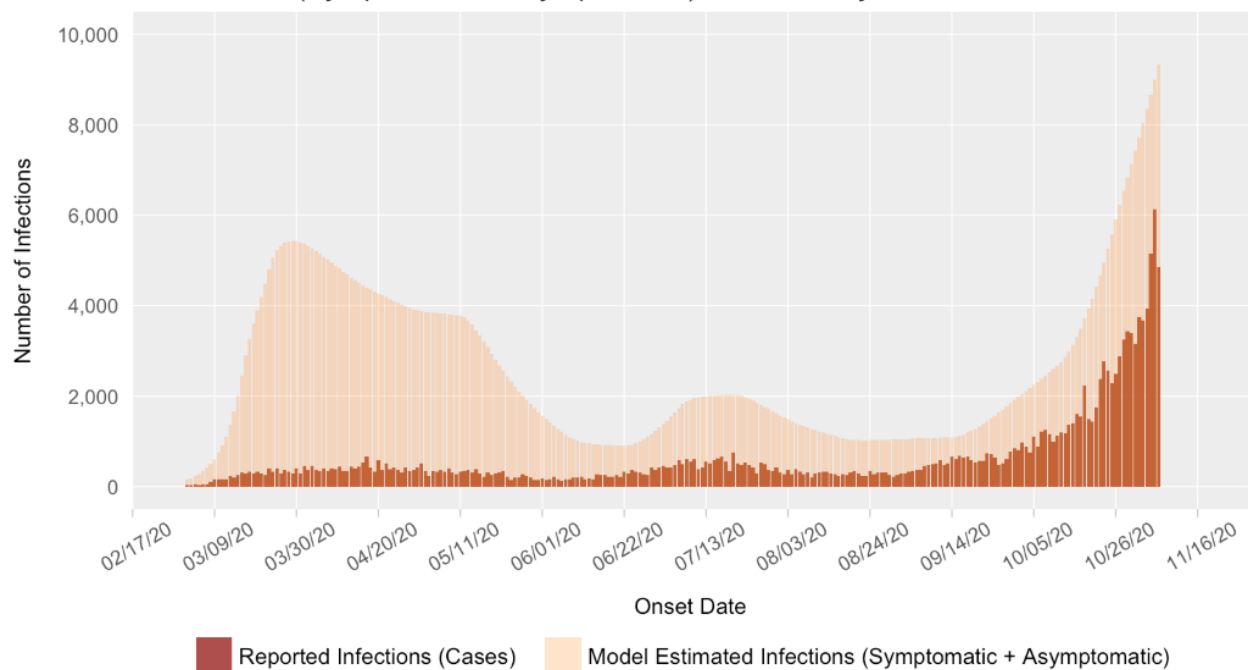
Estimated Proportion of SARS-CoV-2 Infections Detected by State Surveillance Systems
7-Day Moving Average
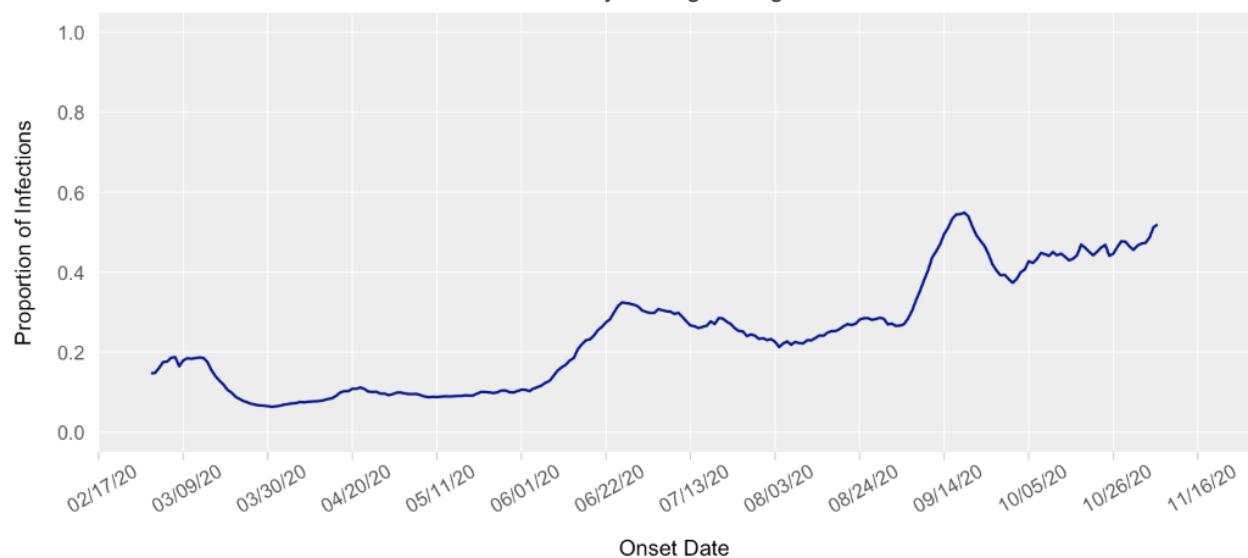
Figure 3. Estimated daily number of new (incident) SARS-CoV-2 infections based on the state-wide SEIR model (light orange graph) and reported cases (dark orange graph) over time shown in the top panel. Lower panel shows the 7-day moving average of the estimated proportion of SARS-COV2 infections that are being captured by Colorado state surveillance systems, over time. The proportion detected is estimated by dividing the total number of new cases captured by state surveillance systems by the model-estimated number of new infections each day. The number of cases captured by state surveillance systems is the number of cases reported by CDPHE, using the onset date of symptoms (if onset date is not available, onset date is imputed by CDPHE using a proxy distribution of recent onset dates). Data are shown through 11/07.

Estimating the current state of SARS-CoV-2 transmission

We use estimates for β and TC to drive the SEIR models and generate model output that can be used to estimate the effective reproductive number, the prevalence of infections and the number of people recovered to date. Estimates are generated for the last day of observed data. Because we base our parameter estimates primarily on COVID-19 hospitalization data, and infections may occur two weeks prior to hospitalization, these estimates don't reflect major changes in transmission that occurred in the prior two weeks. Hospitalizations today generally reflect infections occurring two weeks ago.

Effective reproductive number (R_e). We estimated the effective reproductive number (R_e) from the model output of the number of exposed and infectious individuals, giving a partially smoothed estimate akin to the methods of [17]. For a given point in time, *t*, we estimate Re by calculating the four-day average number of individuals newly exposed on a given day, divided by the number of infectious individuals three-days prior, divided by the length of the infectious period (γ):

$$R_e = \frac{\sum_{i=1}^{4} \frac{E_{ti}}{\alpha}}{\sum_{i=1}^{4} \frac{(I_i + A_i)_{t-\alpha-1}}{\gamma}}$$

Here E_{ti} is the number of exposed individuals at a given time, *t,* in age group *i*; α is the length of the incubation period, I_i and A_i are the number of infected symptomatic and infected asymptomatic individuals in age group *i*, respectively.

Prevalence of infections. The number of infectious individuals at a given point in time is estimated by summing the number of symptomatic infected individuals (I) and asymptomatic infected individuals (A) at time *t*.

The proportion of the population recovered. The proportion of the population recovered at a given point in time is estimated by dividing the cumulative number of individuals recovered by the total population.

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. Estimates of infection prevalence and the proportion of the population recovered are sensitive to model assumptions, which include: the probability an infected individual will be symptomatic and require hospital care; estimated length of hospital stay, which varies over time and by by age.

In the current model, we assume individuals have durable immunity following infection. In reality, our understanding of immunity to SARS-CoV-2 is incomplete and we do not yet fully understand whether immunity wanes over time, how immunity varies among previously infected populations and the extent to which other coronavirus infections confer immunity [18]. 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 [19, 20]. Lastly, our model does not directly account for seasonal impacts on transmission. The magnitude of any seasonal impact is not

well characterized [21, 22] but if present, may slow transmission in the summer months and accelerate transmission in the winter months.

Code

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

Appendix

Table A1. The population by age for each region. Data provided by the Colorado Demography Office. Jefferson plus includes Clear Creek and Gilpin county due to small population sizes.

	Age 0 to 19	Age 20 to 39	Age 40 to 64	Age 65+
LPHA Region				
Central	212732	247551	235110	115027
Central Mountains	39694	56579	59816	26600
East Central	9959	10643	14788	7642
Metro	781805	993164	1059073	457752
Northeast	200376	223385	226804	114700
Northwest	50370	51205	62623	39103
San Luis Valley	12707	10931	13668	9166
South Central	55518	61585	75058	51035
Southeast	11296	12281	14261	9100
Southwest	23288	23453	33674	21739
West Central Partnership	24243	23756	34372	24468
Selected Counties				
Adams	148224	166969	156081	57583
Arapahoe	168400	196144	207357	93087
Boulder	73927	97969	107674	51408
Broomfield	17533	22381	22584	10329
Denver	152802	262391	231012	91649
Douglas	89899	89363	129501	45568
Jefferson plus	131020	157947	204864	108128
El Paso	198325	231427	209421	98181

Table A2. The estimated the rate of infection, β, for each region. β was estimated by fitting model output to observed hospitalizations in the early phase of the epidemic before the implementation of the state-wide stay at home order. In regions with small populations and few hospitalizations during this period, β was estimated using by fitting model output to reported cases adjusted for the proportion of infections detected.

	β	Fit using hospitalization or case data

LPHA Region		
Central	0.3376	Hospitalization
Central Mountains	0.303	Hospitalization
East Central	0.2577	Hospitalization
Metro	0.4102	Hospitalization
Northeast	0.3554	Hospitalization
Northwest	0.2346	Hospitalization
San Luis Valley	0.2043	Hospitalization and Case data
South Central	0.2671	Hospitalization
Southeast	0.2117	Hospitalization and Case data
Southwest	0.2023	Hospitalization and Case data
West Central Partnership	0.2597	Hospitalization and Case data
Selected Counties		
Adams	0.338	Hospitalization
Arapahoe	0.3539	Hospitalization
Boulder	0.2972	Hospitalization
Broomfield	0.2381	Hospitalization
Denver	0.3673	Hospitalization
Douglas	0.3045	Hospitalization
Jefferson plus	0.3276	Hospitalization
El Paso	0.3303	Hospitalization

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