COVID-19 in Colorado, 4/20/2022

Prepared by the Colorado COVID-19 Modeling Group

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Key Messages

- We estimate that approximately 1 in 375 Coloradans are currently infected with SARS-CoV-2 as of April 12.

- BA.2 now accounts for the majority of SARS-CoV-2 infections in Colorado. BA.2 is more transmissible than BA.1 and likely similar to BA.1 in terms of disease severity and immune escape.

- BA.2 may cause an increase in COVID-19 cases and hospitalizations in the next three months, and this increase may have already begun. Hospitalization peaks are projected to be well below prior peaks. BA.2 is also likely to increase the number of counties with Centers for Disease Control and Prevention (CDC) community levels of medium and high.

- The increase in percent positivity and SARS-CoV-2 detection in wastewater over the past month indicate recent growth in infections. COVID-19 hospital demand has been at very low levels; however, it has increased slightly in the past week.

- Modeling scenarios show that future variants could lead to surges in cases and in COVID-19 hospital demand. The severity of the modeled surges depends on the infectiousness, virulence, and immune escape characteristics of the variant.

- Surveillance for variants and for SARS-CoV-2 generally is key to early detection and response.

Introduction

What does the future of SARS-CoV-2 look like in Colorado? By March 2022, COVID-19 hospital demand and reported cases reached pandemic lows and a number of transmission control measures were relaxed across the state. We have previously estimated high levels of immunity in the Colorado population following the Omicron wave, which added infection-acquired immunity for a large number of Coloradans to that from vaccination. However, emerging variants remain an ongoing challenge. Over the past month, BA.2 has become the dominant variant in the US and Colorado, specifically, and there are now signs that SARS-CoV-2 infections may be increasing in Colorado as percent positivity and detection of SARS-CoV-2 in wastewater have ticked upwards in recent weeks.

The purpose of this report is to describe the likely course of SARS-CoV-2 in the coming months. We focus on three key questions:

1. What is the likely impact of BA.2 on SARS-CoV-2 infections and hospitalizations in Colorado?
2. What percent of the Colorado population is estimated to be immune to infection and how will this figure change over time?
3. What are the potential impacts of a future variant?

To answer these questions, we used COVID-19 hospital, vaccination, and case data and a mathematical model of the virus tailored to Colorado. We conducted a review of the emerging literature on BA.2 to assess what is known about the infectiousness, immune escape and virulence of this variant and incorporated that information in model simulations. We also gathered information on Paxlovid treatment in Colorado to account for the impact of access to this treatment on hospital demand and mortality in our model simulations. Details on our model and how we account for Paxlovid access are provided in the Appendix.

Key message 1. COVID-19 hospital demand is at a pandemic low, but there are recent signs that infections may be increasing.

Severe disease has been at pandemic lows. COVID-19 hospital demand, a proxy for the amount of severe disease, has been at a pandemic low in Colorado. As of April 12, 2022, there were 77 people in Colorado hospitalized with COVID-19, the lowest count since March 2020.

We also estimate that the number of people currently infected with SARS-CoV-2 is low. We estimate that 1 in 375 Coloradans (about 0.3%) are infected with SARS-CoV-2 as of April 12, 2022 (Figure 1). We estimate infection prevalence based on hospital demand, which is generally a more stable, albeit lagging, indicator of the amount of SARS-CoV-2 in the population than case counts. However, there are several signs that the true prevalence of infection may be higher than our estimate of 1 in 375. Actual COVID-19 hospital demand has increased a few days earlier than our model projections. In addition, there are indications from the testing and wastewater data that infections may have increased over the past few weeks, as we discuss below.
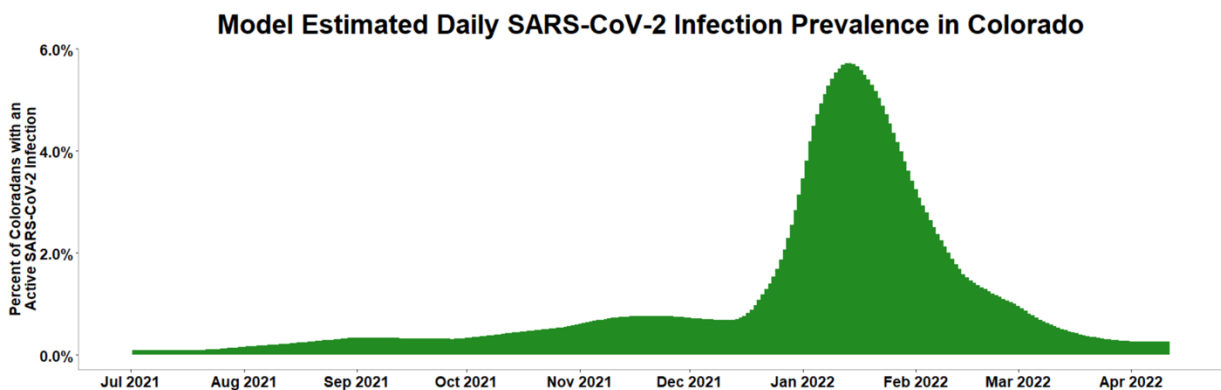

Figure 1. Estimated prevalence of SARS-CoV-2 infection in Colorado from January 2021 to present. The number of infectious individuals is inferred using the SEIRV model and COVID-19 hospitalizations.

There are recent signs that infections are increasing in Colorado. Percent positivity has increased from a low of 2.6% (7-day moving average) on March 18, 2022, to 4.8% as of April 18, 2022. Over the past week, the number of people hospitalized with COVID-19 increased from 77 last week to 88 as of April 19, 2022. Wastewater data also indicate increasing infections, as described below.

Signs of increasing SARS-CoV-2 in wastewater. The concentration of SARS-CoV-2 in wastewater is another useful indicator of epidemic trends. Wastewater analyses measure the number of SARS-CoV-2 copies per liter in wastewater samples obtained at various sites across the state. While wastewater concentrations correlate with case rates (see report on 02/16/2022), the CDC recommends not attempting to translate wastewater concentrations into an estimate of prevalence. To examine the SARS-CoV-2 concentrations in wastewater, we first average readings across multiple sites within a local public health agency (LPHA) region. Second, we calculate the moving average over a window of three samples (approximately once every three days) to smooth the data and reduce the inherent variation in wastewater samples. Figure 2 shows that wastewater concentrations have declined significantly since the Omicron wave peak. However, wastewater concentrations are increasing in several regions across the Front Range including Central, Metro, and Northeast. Note that the vertical axis in Figure 2 is log scale.
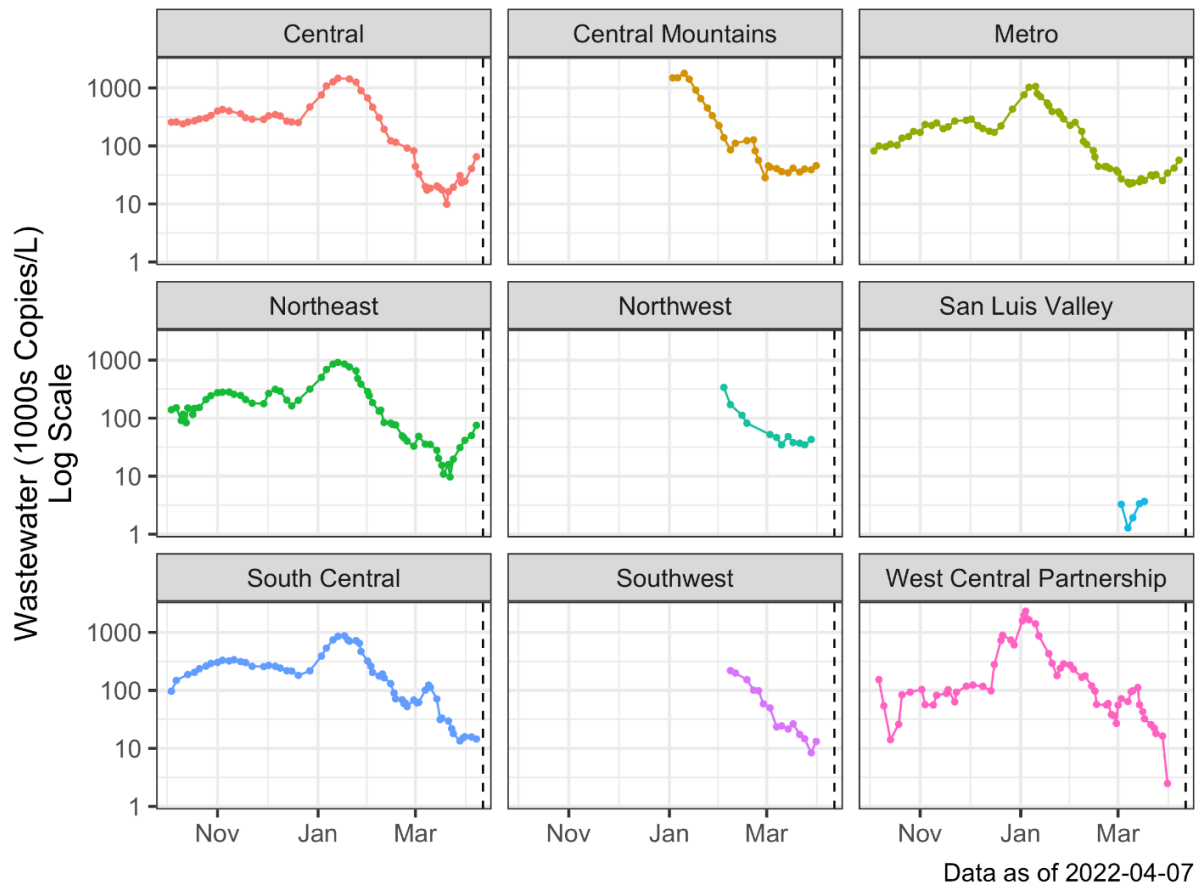

Data as of 2022-04-07

Figure 2. Trends of SARS-Cov-2 in wastewater for Colorado LPHA regions that sample wastewater. Wastewater samples measure the number of SARS-CoV-2 copies per liter in a wastewater sample at various sites across the state. We average daily measurements of sites within a region and then calculate a 3-sample moving average to reduce variation over time. Note that wastewater analysis is expanding to new regions of the state so that earlier data may be missing from some regions. Data source: https://covid19.colorado.gov/covid-19-monitoring-in-wastewater

Key message 2. BA.2 could cause an increase in COVID-19 cases and hospitalizations in the next three months, but hospitalization peaks are projected to be well below prior peaks.

What we know about BA.2. BA.2, a sublineage of the Omicron variant, is a variant of concern that has a growth advantage over BA.1 (UKHSA, 3/23/2022). BA.1 is the sublineage of the Omicron variant that was the primary source of infections in January 2022. As of April 2022, approximately 75% of SARS-CoV-2 infections in Colorado are estimated to be BA.2 infections (CDPHE). Studies have found evidence that BA.2 is more infectious than BA.1. For example, contacts of BA.2 cases are 25-30% more likely to be infected than BA.1 (UKHSA, 3/11/2022). Another study estimated that household contacts of BA.2 have a secondary attack rate of 34% higher than that for BA.1 (Lyngse et al preprint). In the United Kingdom, the growth rate of BA.2 is estimated to be approximately 1.8 times greater than that of BA.1 (UKHSA, 3/11/2022, UKHSA 3/25/2022).

Otherwise, the variant appears similar to BA.1, based on the evidence to date. Immune escape is likely similar to BA.1. Infection with BA.2 can occur after BA.1 infection but it is rare (UKHSA 3/25/2022, Stegger et al preprint). Vaccine effectiveness is likely similar to that for BA.1 (UKHSA, 3/24/22, see Figure 2). A recent test-negative case-control study from the UK showed similar vaccine effectiveness for BA.1 and BA.2. Information on virulence is limited but there is no evidence of increased severity, leading to the assumption that the virulence of BA.2 is similar to BA.1.

Key assumptions for model projections. We used the above scientific evidence to generate a set of projections of the potential future course of SARS-CoV-2 in Colorado accounting for BA.2 becoming the dominant variant. In these simulations, BA.2 is assumed to be 1.3 times as infectious as BA.1 and to have the same virulence and immune escape as BA.1. Due to the high levels of uncertainty, we ran projections with assumptions of infectiousness ranging from 1.3 to 1.8 times greater than for BA.1. In the models, we include three scenarios of infectiousness: 1.3, 1.5, and 1.8 times greater infectiousness for BA.2 versus BA.1.

In the modeling we assume BA.2 was first introduced in mid-December. To fit to current Colorado sequencing data, we varied the rate at which BA.2 was introduced across the different scenarios, from 1 case every 5 days, in the most infectious scenario, to 12 cases per day, in the least infectious scenario. (Note that BA.2 was first detected in South Africa in November, and the first known case in Colorado occurred in late-December.)

In all scenarios, we assume roughly 25% of SARS-CoV-2 infections are due to BA.2 in late March. Since these projections were generated, CDPHE variant tracking data now indicates that 75% of infections are likely due to BA.2 by late March. Thus, actual growth has been more rapid than our modeled growth.

We use the same assumptions about infection-acquired immunity, vaccine-acquired immunity and immune decay as in our February model scenarios. In these scenarios, we assume no additional variants of concern will emerge in the next 12 weeks.

Projected hospitalizations through June 2022. Hospital demand is projected to increase in the weeks ahead (Figure 3). The rate of growth and the peak demand depend both on the characteristics of the BA.2 variant and on the extent to which transmission control measures continue to relax. In these scenarios, peak demand is expected to be well below prior peaks.
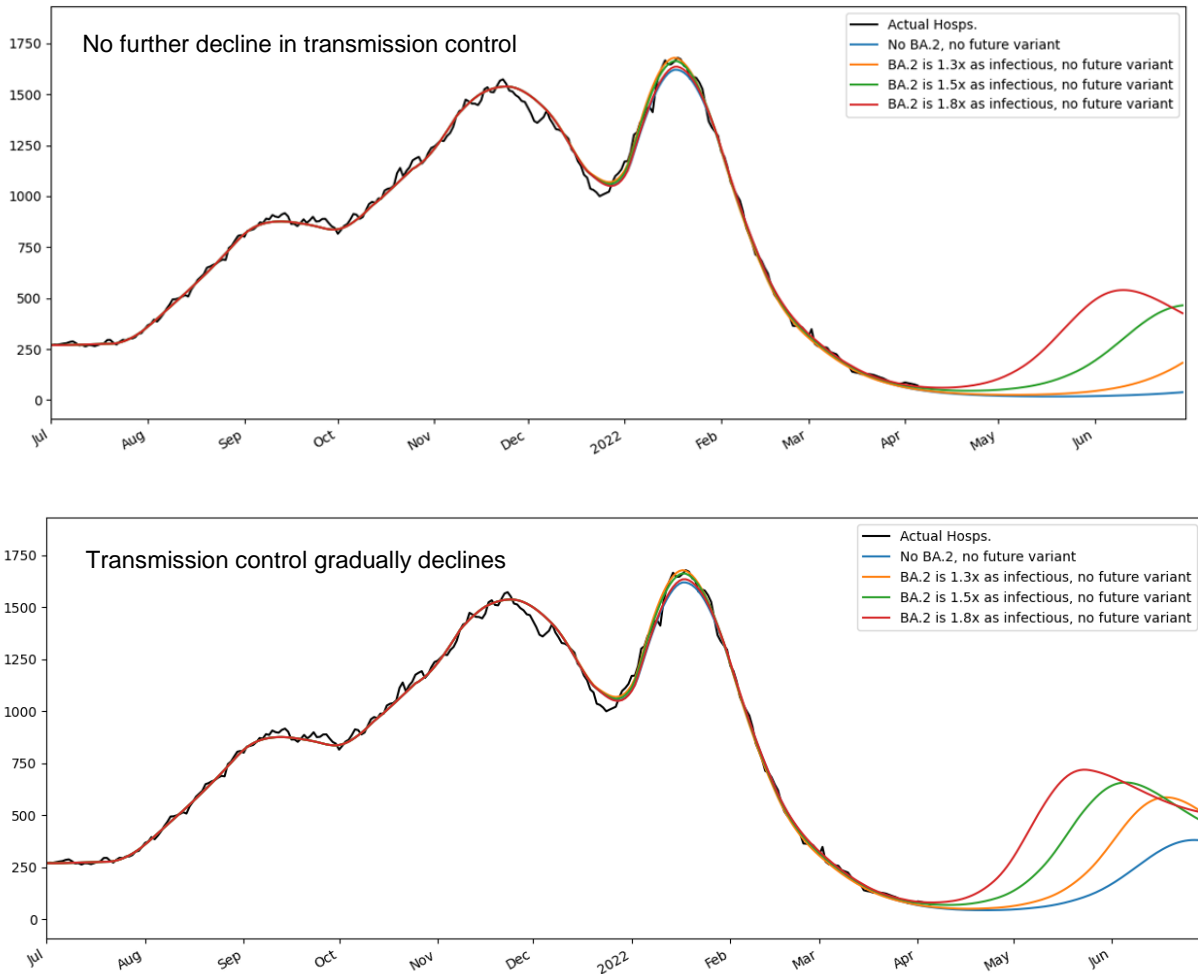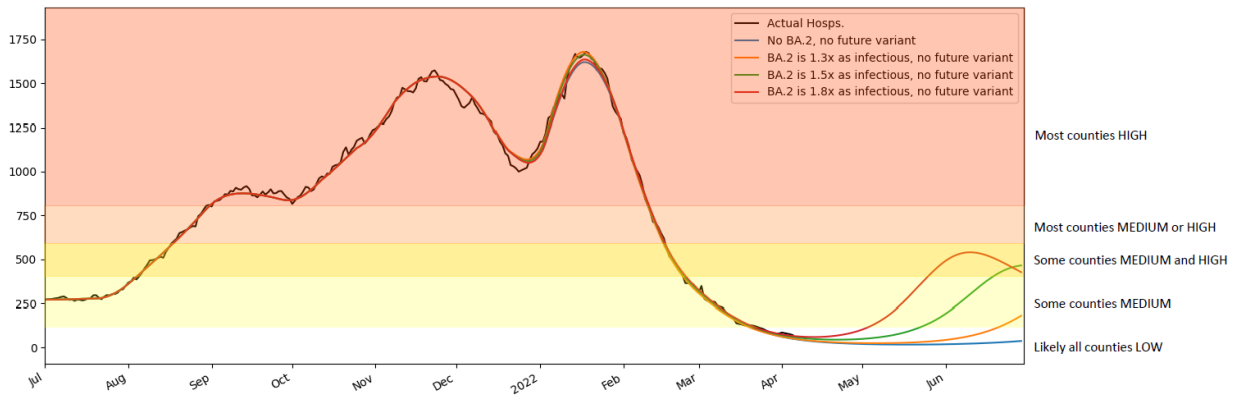
Figure 3. Projected COVID-19 hospital demand in Colorado through June 2022. The top panel shows projected demand if there were no further changes in transmission control. The bottom panel shows projected demand if transmission control were to gradually decline to the lowest estimated value over the course of the pandemic. In each plot, the lines reflect different assumptions about the infectiousness of BA.2 from 1.3 times as infectious (orange) to 1.8 times as infectious (red). Blue shows the projected trajectory if there were no BA.2.

Projected infections through June 2022. In these scenarios, we project that some communities could have COVID-19 Community Levels that are medium or high over the next 12 weeks, as defined by the CDC (Figure 4). As a guide to interventions, the CDC recommends masking for high-risk populations in counties at medium levels, and masking indoors for everyone in counties at high levels.

With <u>no projected shift in transmission control</u>...

With <u>transmission control gradually declining</u> to its lowest point over the course of the pandemic...
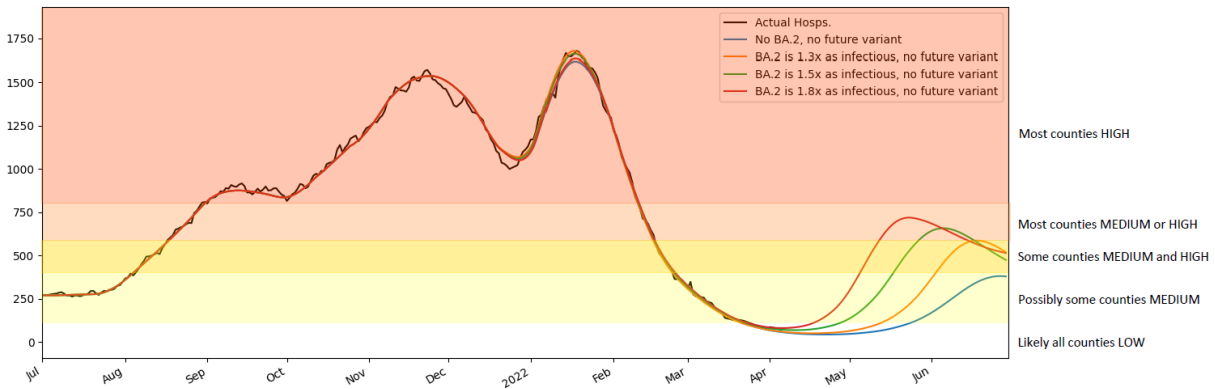

Figure 4. Historical and projected COVID-19 hospital demand in Colorado and the likely distribution of Colorado counties by CDC Community Levels. The top panel shows projected COVID-19 hospital demand if there were no further changes in transmission control. The bottom panel shows projected demand if transmission control were to gradually decline to the lowest estimated value over the course of the pandemic. In each plot, the lines represent different assumptions about the infectiousness of BA.2 from 1.3 times as infectious (orange) to 1.8 times as infectious (red). When hospitalization levels are in the dark yellow bands, some counties are estimated to be classified as Community Level medium or high. When hospitalization levels are in the light pink bands, most counties are likely to be classified as Community Level medium or high.

This analysis is based on a historical analysis of state-level hospital demand vs. the distribution of counties in CDC's low, medium, and high Community levels using the current definitions (Figure 5). Historically, when statewide hospitalizations rose above 400, a few counties entered the medium or high level. When statewide hospitalizations have been above 600, the majority of counties have been in the medium or high categories. At times when there were above 800 hospitalizations, most counties were in the high category. A supplemental analysis accounting for the population in each county yielded similar results.
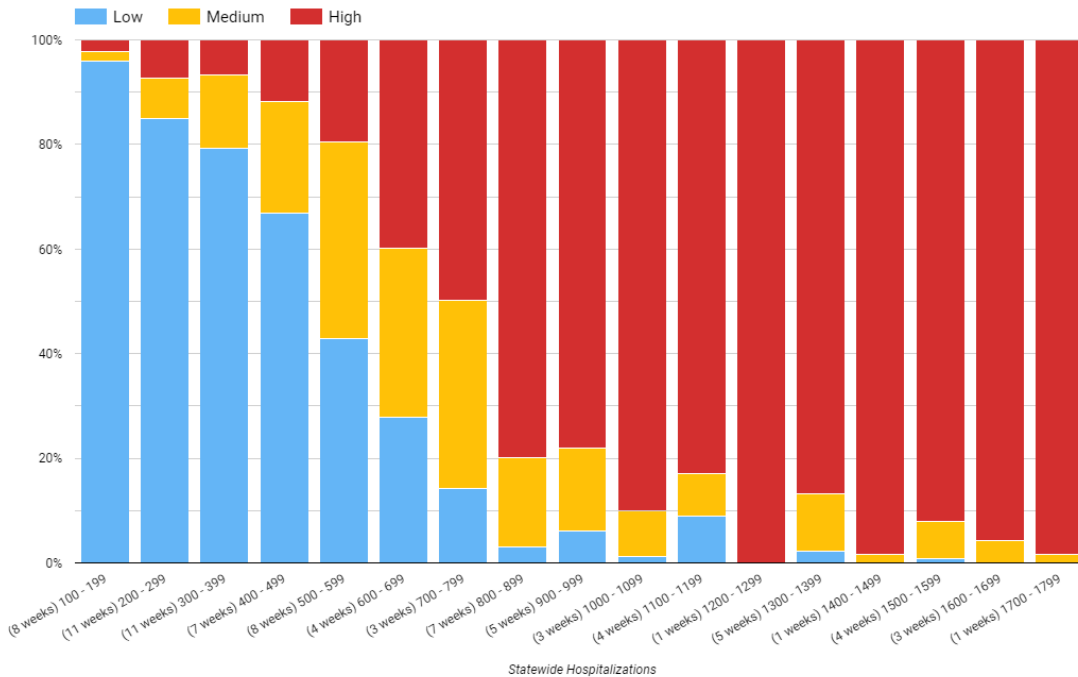
Figure 5. The percent of Colorado counties with low (blue), medium (yellow), or high (red) COVID-19 Community Levels based on CDC classifications vs. state-wide COVID-19 hospital demand throughout the pandemic. Text in parentheses on the x-axis indicates number of weeks that Colorado had a given number of hospitalizations. Analysis based on data from July 31, 2020 to April 5, 2022.

The potential impact of BA.2 on immunity. Generally, population immunity to SARS-CoV-2 wanes over time. If BA.2 does continue to cause an increase in infections in Colorado, the rise in infections may counter the impact of waning immunity over time (Figure 6).
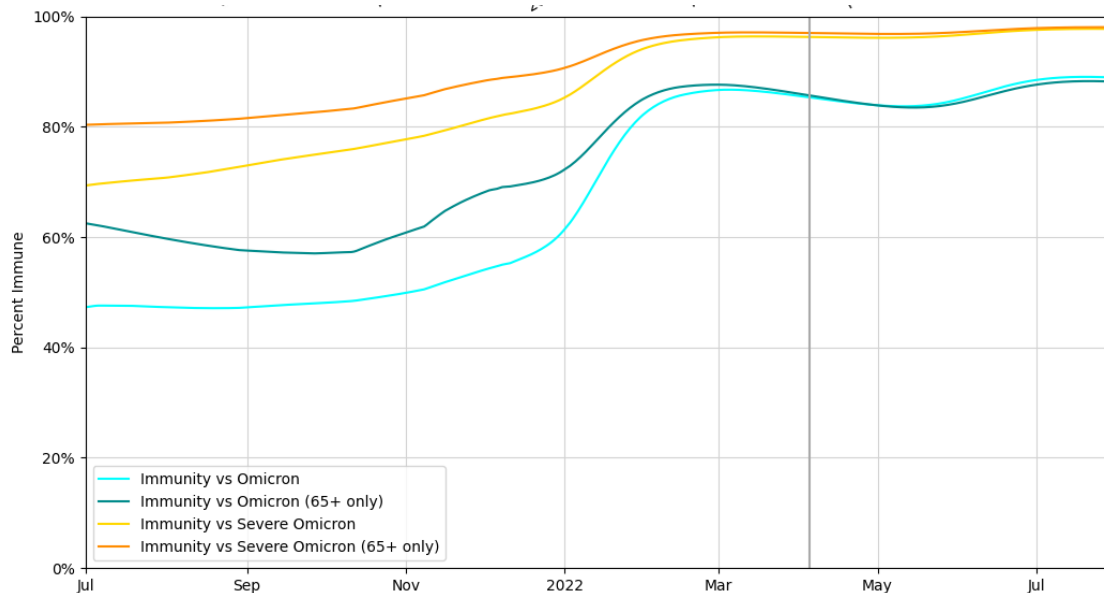

Figure 6. Estimated population-level immunity to infection and severe disease in Colorado, including the full population and those age 65 and older, accounting for a projected BA.2 wave.

Key message 3. Modeling scenarios show that future variants could lead to surges in cases and in COVID-19 hospital demand. The severity of the modeled surges depends on the infectiousness, virulence, and immune escape of the variant.

Key features of variants. As the SARS-CoV-2 virus continues to evolve through mutation, we expect new variants to emerge. While there are many unknowns about what future variants will emerge, there are four key features of new variants to consider in modeling their consequences:

1. **Infectiousness.** More infectious variants spread more efficiently from infected to susceptible populations. The major variants to date have been more infectious than the prior variants that they replaced.

2. **Virulence.** More virulent variants increase the probability of severe disease and death if an infection occurs. Delta was more virulent than prior variants. Omicron was less virulent.

3. **Immune escape.** High immune escape means vaccines and prior infection confer lesser protection against infection. Omicron had relatively high immune escape.

4. **Timing.** When does the variant arrive? Immunity in the population is high now but will decline over time, depending on vaccination and whether another surge takes place

Hypothetical variant scenarios. In order to explore potential impacts of future variants on hospital demand and infections, we created two hypothetical variant scenarios.

Hypothetical Variant A is a variant with high infectiousness and low immune escape. This hypothetical variant is 1.5 times more infectious than BA.2. We assume prior omicron (BA.1 or BA.2) infection confers immunity to infection and vaccines perform similarly in their effectiveness against Omicron.

Hypothetical Variant B is a variant with the same infectiousness as BA.2 and high immune escape. This hypothetical variant is similar to BA.2 in terms of infectiousness. But there is high immune escape, akin to what was seen with Omicron in December/January, such that there is weak cross-variant immunity. In this case, prior Omicron infection (BA.1 or BA.2) does not confer much protection against infection. Vaccines confer similar protection as they did to Omicron.

For each of these scenarios, we considered three different levels of disease severity: decreased severity (half as severe as Omicron), same severity as Omicron, and increased severity (2x as severe as Omicron).

For simplicity, each variant is assumed to arrive in CO on 04/15/22. We assume that rising cases and hospitalizations do not shift behavior or lead to adoption of control policy measures. In these projections, we assume continued growth of BA.2 in CO, and that BA.2 is 1.5x as infectious as BA.1. Models account for the availability of antiviral treatments (see Appendix).

These scenarios do not represent the full range of possible future variants with regard to key characteristics but offer a range of illustrative examples. For further discussion of potential future variant scenarios, see WHO, McKinsey, and UKHSA.

Potential impacts on hospital demand. The introduction of a variant with high infectiousness and low immune escape would lead to a surge in hospital demand (Figure 7). Demand is projected to be well below prior peaks, with the magnitude of the peak higher for a more virulent variants. In contrast, the introduction of a variant with similar infectiousness to BA.2 and high immune escape is projected to put

a much greater strain on the hospital system (Figure 8). If severity of the disease caused by the variant is similar to or worse than that caused by Omicron, we could see a peak similar to or greater than prior peaks.

Projected prevalence. A variant with infectiousness similar to BA.2 and high immune escape could lead to infection prevalence higher than seen previously, even in scenarios in which hospital demand remains below prior peaks (Figure 9). We note the estimated prevalence is the same regardless of assumptions about the virulence of variants A and B in our models. Virulence has a strong impact on hospital demand, but does not directly impact the spread of infections (until high hospital demand prompts a change in behavior or policy).

Caveats. These are hypothetical scenarios – in reality, we are unsure what will be the characteristics of the next variant and when it will emerge. Further, while it is clear that immunity wanes over time, there remain large uncertainties about cross-variant immunity, the rate of decay in immunity and the durability of protection against severe disease conferred by vaccination and prior infection. Historically we have seen that transmission control behavior and policies change when reported cases and hospital demand increases. We do not account for changes in behavior or implementation of policies to slow transmission in our models.

Conclusions. Future variants could lead to surges in cases and COVID-19 hospital demand. While the timing and characteristics of the next variant are uncertain, the greatest challenge to our health care system could come from a variant with high immune escape and high virulence. Under such scenarios there may be an intense need for treatments (if effective) and hospital beds. A variant with high immune escape and/or high infectiousness could lead to many infections, necessitating surge testing capacity and treatments for vulnerable populations.
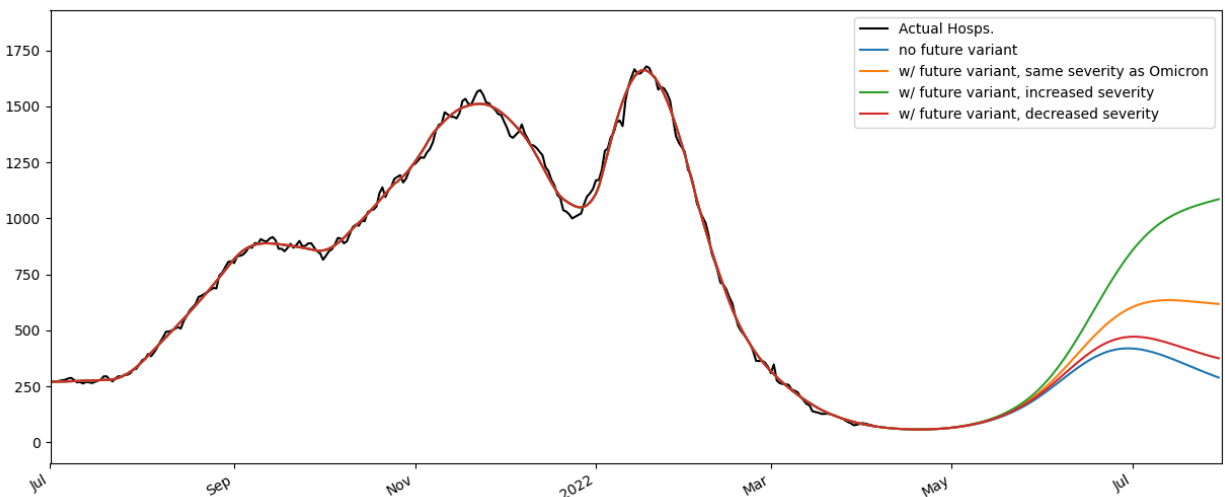

Figure 7. Projected future hospital demand for hypothetical variant A, a variant with high infectiousness and low immune escape. Hospital demand is shown for three different levels of virulence for the variant, high virulence (green), same as omicron (yellow), and decreased severity (red). The blue line shows projected hospital demand in the absence of this variant, accounting for the growth of BA.2. Projections are provided through July 2022 with the caveat that there is considerable uncertainty in projections for late June and July.
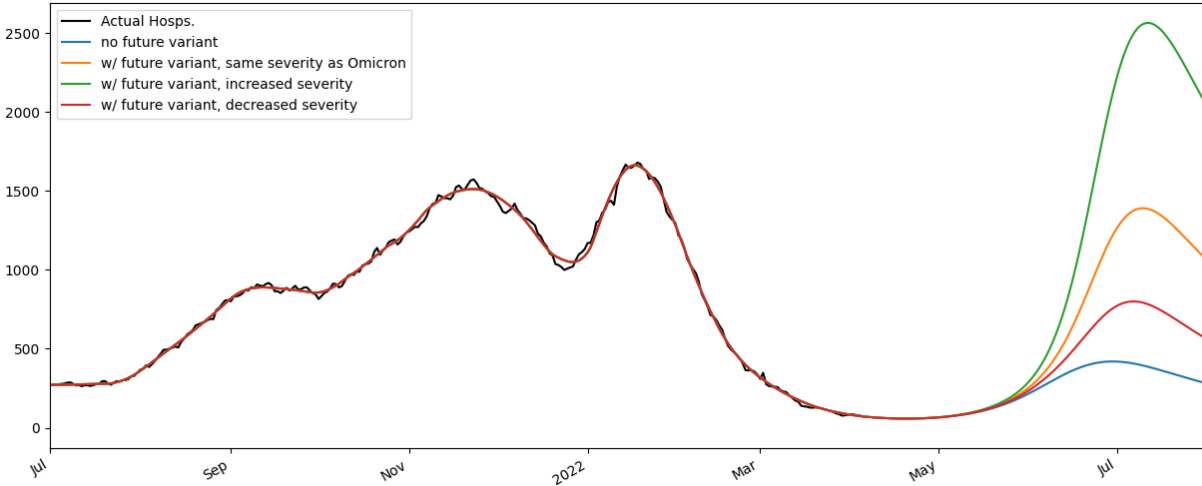
Figure 8. Projected future hospital demand for hypothetical variant B, a variant with the same infectiousness as BA.2 and high immune escape. Hospital demand is shown for three different levels of virulence for the variant, high virulence (green), same as omicron (yellow), and decreased severity (red). The blue line shows projected hospital demand in the absence of this variant, accounting for the growth of BA.2. Projections are provided through July 2022 with the caveat that there is considerable uncertainty in projections for late June and July.
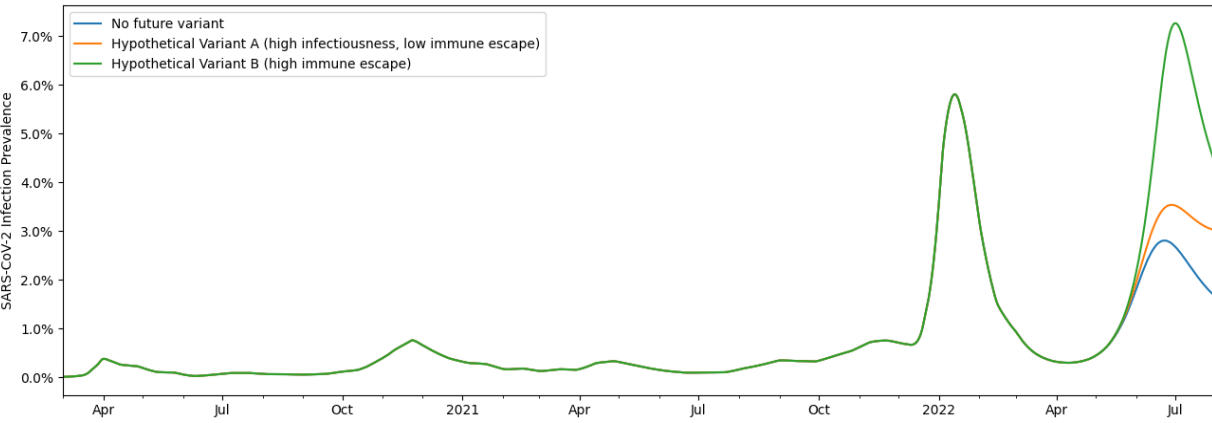

Figure 9. Projected prevalence for hypothetical variant A, a variant with high infectiousness and low immune escape (orange line), and hypothetical variant B, a variant with the same infectiousness as BA.2 and high immune escape. The blue line shows projected hospital demand in the absence of this variant, accounting for the growth of BA.2.

Next steps

It will be crucial to monitor the growth of BA.2 in Colorado, including the extent to which COVID-19 hospital demand tracks with our projections. More broadly, surveillance for variants and SARS-CoV-2 generally are critical for early detection and an appropriately measured response to control surges. We continue to track other emerging variants with the expectation that new variants will emerge. This report demonstrates that models are available to project the course of future variants as they are identified.

Appendix

The model is an age-structured SEIRV (susceptible-exposed-infected-recovered-vaccinated) infectious disease transmission model that has been calibrated to Colorado-specific data whenever possible. For example, the length of time that a COVID-19 patient is assumed to spend in the hospital varies by age and over time and is based on data provided by Colorado hospitals. Code is available on GitHub at https://github.com/CSPH-COVID/covid-models.

This report is based on COVID-19 hospitalization data through 4/05/2022 and vaccination data through 04/01/2022.

Recent model updates

Paxlovid treatment. The model now includes decreased case severity due to treatment of high-risk adults with Paxlovid. We used data provided by CDPHE as well as a review of the scientific literature to develop the following assumptions in our model

- In mid-January, roughly ~1% of confirmed cases received Paxlovid
- In mid-February, roughly ~5% received Paxlovid
- In mid-March, and going forward, roughly ~10% receive Paxlovid
- Those treated with Paxlovid are at higher-risk than the average COVID case. Without Paxlovid, they'd be 2x more likely to be hospitalized than the average person.
- Paxlovid treatment reduces the chances of hospitalization and death by 89%

COVID-19 hospitalization rates. We have adjusted assumptions of hospitalization rates in 2020 to reflect current understanding of hospitalization reporting systems.

Hospitalization data used for fitting. Last month, we integrated data from COPHS with EMResource to account for additional hospitalizations that have been backfilled or that we expected to be backfilled in the following months, leading to higher overall estimates for the number of individuals hospitalized with COVID-19. Due to data alignment issues, we have reverted to using EMResource for COVID-19 hospitalizations in Colorado.

We have not yet included fourth vaccinations in our model. Work is underway to include these in future reports.