COVID-19 in Colorado, 10/06/2022

Prepared by the Colorado COVID-19 Modeling Group

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Key Messages

- Surveillance data paints a mixed picture of COVID-19 in Colorado. COVID-19 hospital demand
 has increased this week, while SARS-CoV-2 wastewater concentrations indicate a slow decline in
 infections statewide, and percent positivity has plateaued. There are areas of the state where
 wastewater data indicate an increase in infections. In comparison with past peaks of the
 pandemic, COVID-19 hospitalizations are relatively low (<200 compared to over 1600 during the
 January 2022 peak).
- Model simulations continue to indicate a decline in COVID-19 hospital demand over the next 12 weeks in the absence of a new variant. These projections account for current trends in bivalent booster uptake and are consistent with model simulations by the COVID-19 Forecast Hub.
- There are several emerging variants we are watching, but information is limited. BF.7 has a growth advantage over BA.5 and increased immune escape. BQ.1 has recently emerged, but key characteristics including growth advantage and immune escape, are unknown.
- Model simulations that include a hypothetical variant with high immune escape, entering Colorado in late September, indicate a rise in hospital demand by the end of 2022. The increase in hospital demand will be steeper if the new variant also has greater virulence relative to current variants.
- The uptake of the bivalent booster is highest in older age groups and thus far, has been slower than uptake of prior boosters.
- Bivalent boosters can prevent infections and hospitalizations. The future benefit of bivalent boosters depends on booster uptake and the characteristics of the next variant.

Introduction

Colorado experienced a wave of SARS-CoV-2 infections and COVID-19 hospital demand during the summer of 2022. Hospital demand was well below prior peaks (reaching 324 patients in July versus over 1600 in January 2022); however, we estimate that many Coloradans were infected, as reported in our August 25, 2022 report.

In this report, we consider the possible course of COVID-19 over the fall months ahead. We focus on the potential impact of emerging variants as well as the benefit of the recently approved bivalent COVID-19 booster. We describe the literature on emerging variants of concern, as well as the effectiveness of the bivalent booster. We present information on booster uptake in Colorado to date. And we show a series of projections of COVID-19 hospital demand over the fall, including the potential impact of boosters and of a hypothetical new variant. To make our projections, we used COVID-19 hospital, vaccination, and case data and a mathematical model of the SARS-CoV-2 epidemic tailored to Colorado. Details on the model and updates are provided in the Appendix.

SARS-CoV-2 infections have declined since this summer. They now appear to be declining slowly but some indicators are mixed.

We estimate that the number of people infected with SARS-CoV-2 in Colorado declined since July and the current prevalence of infections is similar to February 2022 (Figure 1). We estimate that approximately 1 in every 188 Coloradans are currently infected with SARS-Cov-2 as of October 6, 2022. These estimates are sensitive to model assumptions, including assumptions about the probability that an infected individual will be symptomatic and require hospital care, which we assume will vary by age.

This picture is consistent with the waste-water data. Statewide, the aggregated concentration of SARS-CoV-2 in wastewater continues to decline (Figure 2). Current levels are similar to concentrations seen in early February.

Some indicators suggest that infections may have plateaued. The percent positivity (the percent of SARS-CoV-2 tests that are positive) has plateaued over the past two weeks. Similarly, SARS-CoV-2 concentrations in wastewater have plateaued in some regions (Figure 3). COVID-19 hospital demand in Colorado remains relatively low but has risen from 145 patients on September 20, 2022, to 185 patients on October 4, 2022. Typically, increases in hospital demand follow increases in wastewater concentrations and percent positivity. It is unclear if the recent rise in hospitalized COVID-19 patients is due to chance or a shift in disease patterns. Notably, hospital admissions continue to decline nationally and in Colorado (CDC Data Tracker).

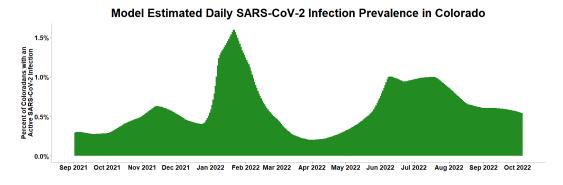


Figure 1. Estimated prevalence of SARS-CoV-2 infection in Colorado from July 2021 to October 6, 2022. The number of infectious individuals is inferred using mathematical model fit to COVID-19 hospitalizations in Colorado.

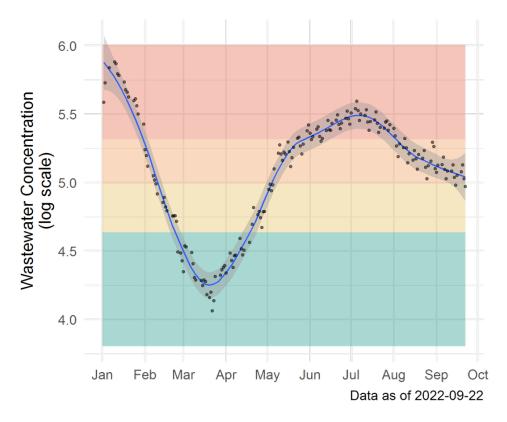


Figure 2. Population-weighted average wastewater concentrations from 53 sites Aug 2021 to September 22, 2022. Bayesian Structural Time Series model is fit to logged measurements from each utility. Population-weighted average is calculated each day. Blue line is a localized regression fitted to a sliding 3-month window. Data source:

 $\underline{https://cdphe.maps.arcgis.com/apps/dashboards/d79cf93c3938470ca4bcc4823328946b}$

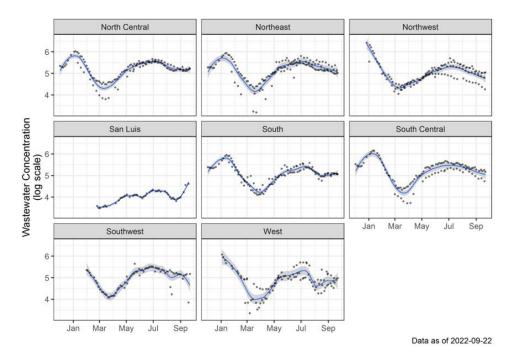


Figure 3. Population-weighted average wastewater concentrations from 8 regions in Colorado from Aug 2021 to September 22, 2022. Bayesian Structural Time Series model is fit to logged measurements from each utility. Population-weighted average is calculated each day. Blue line is a localized regression fitted to a sliding 3-month window. Data source:

https://cdphe.maps.arcgis.com/apps/dashboards/d79cf93c3938470ca4bcc4823328946b

We estimate that there are high levels of immunity against severe COVID-19 disease and infection in Colorado at present (Figure 4). Because vaccines confer strong protection against severe disease, immunity against severe disease is higher than immunity against infection. Due to the recent wave of BA.5 infections, we estimate immunity has increased over the past two months.

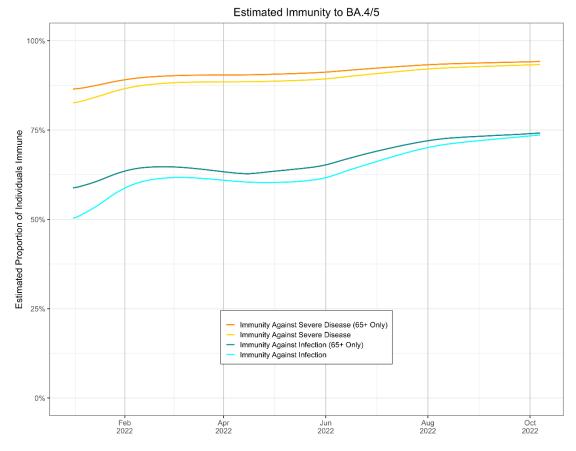


Figure 4. Estimated immunity to BA.5 in Colorado against severe disease and infection among the full population and those age 65 plus.

There are several emerging variants we are tracking. It is unclear what variant will be dominant this winter.

BA.5 remains the dominant variant of concern (VOC) in the U.S., with prevalence steadily decreasing in the last 3-weeks. BA.5 currently accounts for about 80% of infections nationwide (CDC COVID Variant Surveillance). BA.4.6 accounts for about 13% of infections and cases are steadily increasing nationwide (CDC COVID Variant Surveillance). There is a modest growth advantage of BA.4.6 estimated at 2.3% over BA.5 (UK HSA).

Over the month of September, two new Omicron subvariants emerged in Europe and West Africa. Although these subvariants are currently not highly prevalent in the U.S., early reports suggest that BF.7 (also called BA.2.75.2) and BQ.1 may have greater immune escape over BA.1, BA.2, BA.4 and BA.5 variants. BF.7, derived from the parent lineage BA.2.75 which is the dominant circulating variant in India, has been reported in Belgium, Denmark, Germany and France. BF.7 cases account for an estimated 3.4% of infections nationwide (CDC COVID Variant Surveillance). BQ.1, derived from the BA.5 lineage, has been reported in England, France, Nigeria, and the U.S. Early data suggests that the growth advantage for BF.7 is 6% per day over BA.5, while BQ.1 may have the growth advantage, there is insufficient data at present. One study estimated that BF.7's neutralization ability is 6-fold less than BA.5, representing the most neutralization resistant variant evaluated to date (Sheward 2022). BA.5 and BA.4.6 are currently the

dominant VOC in the U.S., but there are predictions that the rising subvariants BF.7 and BQ.1 may be more prevalent in the U.S. by the end of November (covSPECTRUM).

Bivalent booster uptake in Colorado is lower than uptake of the first booster

What we know about bivalent boosters. The bivalent booster is designed to provide protection against infection and severe disease for currently circulating SARS-CoV-2 variants. Results of vaccine efficacy (VE) from Moderna and Pfizer bivalent boosters are not yet available as clinical trials are currently ongoing. However, early clinical data shows an increased antibody response and neutralization activity from the bivalent boosters. An evaluation of the Moderna bivalent booster administered in adults found increased neutralization activity against BA.1 and BA.4/BA.5 strains 29 days following receipt of the bivalent booster (Chalkias NEJM 2022) and similar increases were also observed among older adults who received Pfizer BA.1 bivalent booster (Launay NEJM 2022). Evidence from the administration of monovalent mRNA vaccines and boosters shows initial strong protection against hospitalization and symptomatic infections, followed by declines in VE across all ages in the United States (ACIP 2022). The UK HSA Vaccine Surveillance Report highlights declines in vaccine efficacy against hospitalization due to BA.1 and BA.2 in the months following the administration of the primary mRNA series and monovalent boosters (UK HSA 2022). This is one of the reasons for bivalent boosters, as immunity among those previously boosted is waning over time. This evidence also suggests that if bivalent boosters have similar initial high protection against hospitalizations, there may also be gradual declines in vaccine effectiveness in the forthcoming months.

Bivalent booster uptake in Colorado. We compared the uptake over time of the bivalent boosters to that of the first booster authorized in the fall of 2021. To date, approximately 2% of the Colorado population has received a bivalent booster. This comparison shows a slower uptake of the bivalent booster in comparison to the pace for the first boosters for all adults (Figure 5). While the trajectory of bivalent booster administration may increase over the months to come, we assume that the current trajectory will be maintained in the modeling that follows. The comparison of the trajectory for the bivalent boosters to the first booster points to a need to enhance uptake of the bivalent boosters.

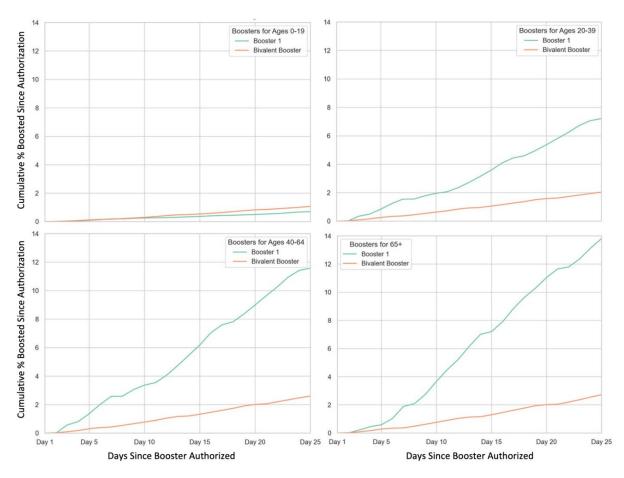
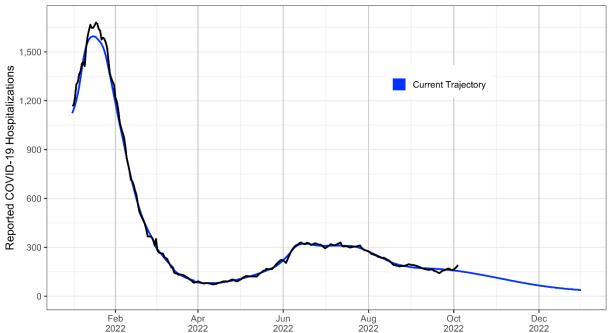


Figure 5. Cumulative percent boosted amongst age groups since booster authorization for booster 1 (blue line) vs. bivalent booster (orange line). Since authorization of booster 1 was staggered based on age and risk status, we only include those who received their booster 1 after the booster was authorized for their age group in our cumulative count. This means Day 0 for booster 1 is 9/22/2021 for age 65+ and 11/21/2021 for those 18-64. The bivalent booster Day 0, accordingly, is 9/06/2022 for all age groups. We note that, for some age groups, booster 1 uptake was already considerable before Day 0.

If a new variant reached Colorado, there could be a rise in hospital demand this fall. Bivalent boosters will prevent infections and hospitalizations.

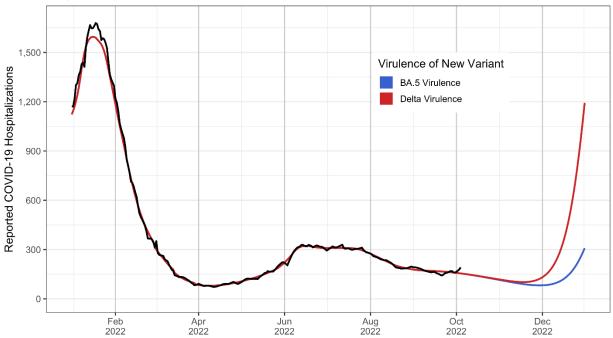
If Colorado continues with the current mix of variants *without* the arrival of a new variant, we project continued decline of the epidemic curve through the end of 2022. On this course, the daily count of hospitalized Coloradans would drop below 50 by year's end. In this scenario, we assume that booster uptake continues at current rates. We also assume that the bivalent booster has the same protective effect as prior boosters. We note that the recent rise in hospital demand deviates from this projection.





What if a new, more virulent variant arrives? A new variant could cause a rise in hospital demand. Below, we show projections of the epidemic curve if a hypothetical new variant with high immune escape were to have reached Colorado in late September. This hypothetical variant is assumed to be as infectious as BA.5 and have a high immune escape to all prior variants, similar to what was observed for BA.5. In the scenarios involving hypothetical variants, the epidemic curve would rise with the steepness and height of the rise depending on the virulence of the variant. The virulence of the hypothetical variant is assumed to be equivalent to that of either Delta or BA.5. If the virus has virulence comparable to that of Delta (the most virulent variant observed in Colorado to date), the hospitalization count rises steeply by December following the arrival of the new variant in late September.





What protection can bivalent boosters offer? Considering these three scenarios—no new variants and new variants with virulence of BA.5 or Delta—we estimate the benefit of bivalent boosters if uptake continues at the current pace compared to no bivalent boosters. The table below shows the potential reductions in numbers of infections and hospitalizations due to bivalent boosters for these scenarios (Table 1). At the current rate of vaccination with the bivalent booster, boosters will prevent infections and hospitalizations. The reductions are relatively modest, reflecting the low rate of booster administration. Increases in bivalent booster uptake, particularly if and when a new variant emerges, will prevent more infections and hospitalizations.

Table 1. The estimated impact of bivalent boosters on SARS-CoV-2 infections and COVID-19 hospitalizations from October 1, 2022, to December 31, 2022, with and without a new, hypothetical variant. We compare the cumulative number of infections if bivalent booster uptake continues at current rates vs. if no bivalent boosters were administered. The hypothetical variant is assumed to have high immune escape and infectiousness similar to BA.5.

	Reduction in infections if current booster uptake continues through the fall		Reduction in hospital admissions if current booster uptake continues through the fall	
	% decrease	n	% decrease	n
No New Variant	5.0%	28,600	4.1%	59
New Variant with BA.5 Virulence	4.2%	48,300	3.9%	78
New Variant with Delta Virulence	3.9%	54,100	3.9%	14

These estimates are sensitive to model assumptions and characterized by a high level of uncertainty. Key sources of uncertainty are the characteristics of the next variant, future bivalent booster uptake and the extent to which the bivalent booster confers protection against the next variant. Our key findings – that in the absence of a new variant, COVID-19 hospital demand should decline in the near-term, that a new variant has the potential to cause a winter wave of infections and hospital demand, and that bivalent booster uptake can prevent infections and hospitalization – are consistent with those of other modelling efforts including the COVID-19 Forecast Hub and the COVID-19 Scenario Modeling Hub.

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 model simulations using COVID-19 hospitalization and vaccination data through 10/04/2022.

Recent model updates

The model has been updated to reflect our understanding of current bivalent booster data and hospital reporting rate. This month, our model includes the following updates:

- We incorporate bivalent boosters in the model data on vaccinations provided by CDPHE. We assume that any first or second booster dose given on or after 09/06/2022 is a bivalent booster, and that earlier boosters were retired beginning on this date.
- Bivalent boosters are assumed to have the same protective effect as prior boosters. The main impact is to increase immunity in populations where immunity has waned.
- We continue to assume a drop in detection and reporting of "with-COVID" hospitalizations after mid-March 2022. This corresponds with a change in SARS-CoV-2 testing protocols at major Colorado hospitals such that all patients are not presumptively screened. Model fitting and projections account for this change. We define the hospital reporting percentage as the number of COVID-19 hospitalizations reported vs. what would have been detected if universal testing on admission still occurred. We estimate hospital reporting to be 80% based on a recent data analysis, phased in incrementally over March 2022.

Model scenarios

We developed scenarios that consider the impacts of bivalent boosters and the emergence of a new, hypothetical variant. These models are based on scenarios developed by the <u>COVID Scenario Modeling</u> Hub, Round 15.

Booster Scenarios. In the booster scenario, we assumed that bivalent booster uptake continues at current rates, using the most recent 7-day average doses by age group, from data provided by CDPHE. As reported above, the current bivalent booster uptake is well below the uptake of booster 1.

In the no booster scenario, we assume that no boosters are administered after 9/06/2022.

Variant Scenarios. We created a hypothetical variant with high immune escape and infectiousness similar to BA.5. Below, we refer to this variant as Variant X. We introduced this variant into the model starting on 9/20/2022 and assume there are multiple introduction events. Because there are uncertainties in how virulent a new variant would be should it emerge, we created a scenario in which Variant X has the same virulence as BA.5 (0.833x the hospitalization rate of the wildtype strain), and a scenario in which Variant X has much greater virulence than BA.5, akin to Delta (2.38x the hospitalization rate of the wildtype strain).

Details of model implementation include

- We introduced the variant at a rate of 5 seeds per day from 09/20/2022 to 10/30/2022, which was the same density and duration used when introducing BA.5.
- Variant X has immune escape characteristics that resemble those used for BA.5 in this model. One important distinction is that for BA.5 and prior omicron variants, we assume immune escape to Omicron variants is lower than immune escape to non-Omicron variants. For simplicity and because it has been ten months since non-Omicron variants were circulating, we assume Variant X has uniform immune escape to all prior variants. Specifically, we assume that for weakly immune individuals, Variant X had 60% immune escape from all prior variants (wildtype through BA.5), derived from the average between the two assumed values of immune escape for weakly immune individuals, which was 80% for pre-Omicron variants and 40% for early Omicron variants. We assume that for strongly immune individuals, Variant X had 9.5% immune escape from all prior variants (wildtype through BA.5), derived from the average between the two assumed values of immune escape for strongly immune individuals, which was 15% for pre-Omicron variants and 4% for early Omicron variants.
- We set most of the biological parameters of Variant X, such as the latent period, symptomatic fraction, and recovery rate, to the default values (i.e., the values assumed for the wildtype strain), however we assume that Variant X is equally as infectious as BA.5.

In total, we modeled six scenarios:

Scenario 1a. Current booster uptake, no new variant.

Scenario 1b. No boosters, no new variant.

Scenario 2a. Current booster uptake, new variant with low virulence.

Scenario 2b. No boosters, new variant with low virulence.

Scenario 3a. Current booster uptake, new variant with high virulence.

Scenario 3b. No boosters, new variant with high virulence.

Estimating the impact of bivalent boosters

We investigated the potential impact of bivalent boosters by looking at cumulative infections and hospital admissions from 10/01/2022 through 12/31/2022 as estimated by the model. We compared estimated cumulative infections and hospital admissions in our counterfactual scenarios (in which all booster doses were set to zero after 09/06/2022) to estimated cumulative infections and hospital admissions in our current booster uptake scenarios. Estimates of the absolute number of cumulative infections and hospitalizations for each scenario are rounded to three significant figures. For cumulative hospital admissions, we first calculated the model-estimated new hospitalizations by age, which was obtained by dividing the age-specific model-estimated daily hospital census by average age-specific length of stay and summed these quantities. Our estimates are sensitive to model assumptions and characterized by a high level of uncertainty.

Table 1A. The estimated number of SARS-CoV-2 infections and COVID-19 hospitalizations from October 1, 2022, to December 31, 2022, with and without bivalent boosters and a new, hypothetical variant. We compare the cumulative number of infections if bivalent booster uptake continues at current rates vs. if no bivalent boosters were administered.

Infections		Hospital Admissions	
No Bivalent	Bivalent	No Bivalent	Bivalent
Boosters	Boosters	Boosters	Boosters

No New Variant	571,000	542,000	1,440	1,380
New Variant with BA.5 Virulence	1,160,000	1,108,000	1,990	1,910
New Variant with Delta Virulence	1,380,000	1,330,000	3,760	3,620