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Supplementary appendix

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Appendix

Implications of suboptimal COVID-19 vaccination coverage in Florida and Texas

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Model structure

We adapted our previous agent-based model of COVID-19 transmission¹ to simulate outbreaks in Florida and Texas since the start of vaccination on December 12, 2020. The model included variants detected in these states including Alpha, Gamma, Iota, and Delta, each of which exceeded cumulative prevalence of 5% in addition to the original Wuhan-I strain.

The natural history of disease was implemented with epidemiological classes for susceptible; latently infected (not yet infectious); asymptomatic (and infectious); pre-symptomatic (and infectious); symptomatic (and infectious) with either mild or severe illness; recovered; and dead. To incorporate age-specific risk of hospitalizations and deaths, as well as contact patterns, we stratified the model population into six age groups of 0 to 4, 5 to 19, 20 to 49, 50 to 64, 65 to 79, and 80+ years based on demographics of each state.² Daily contacts between individuals were sampled from a negative-binomial distribution parameterized (Table S1) using empirical data on pre-pandemic and pandemic-era interactions.^{3,4}

Table A1. Mixing patterns and the daily number of contacts derived from empirical observations.^{3,4} Daily numbers of contacts were sampled from negative binomial distributions for different scenarios.

Age group	Proportion of contacts between age groups					No. of daily contacts without self-isolation Mean (SD)	No. of daily contacts for self-isolated individuals Mean (SD)
	0-4	5-19	20-49	50-65	65+		
0-4	0.2287	0.1839	0.4219	0.1116	0.0539	10.21 (7.65)	2.86 (2.14)
5-19	0.0276	0.5964	0.2878	0.0591	0.0291	16.793 (11.7201)	4.70 (3.28)
20-49	0.0376	0.1454	0.6253	0.1423	0.0494	13.795 (10.5045)	3.86 (2.95)
50-65	0.0242	0.1094	0.4867	0.2723	0.1074	11.2669 (9.5935)	3.15 (2.66)
65+	0.0207	0.1083	0.4071	0.2193	0.2446	8.0027 (6.9638)	2.24 (1.95)

Transmissibility

The per-contact transmission probability of the original Wuhan-I strain of SARS-CoV-2 was calibrated by fitting the model to case incidence data per 100,000 population in Florida and Texas from October 1, 2020, to July 31, 2021.⁵ We chose October 1 as the starting point for our calibration and simulations because it was a time of a relatively low incidence preceding the fall/winter wave in these two states. The calibration resulted in the per-contact transmission probabilities of 0.106 and 0.067 during the pre-symptomatic stage in Florida and Texas, respectively. In Florida, Alpha and Gamma were introduced on December 15, 2020, Iota on January 15, 2021, and Delta on April 4, 2021.⁶ In Texas, Alpha was introduced on July 21, 2020, Gamma on January 17, 2021, and Delta on March 29, 2021.⁷ The transmissibilities of Alpha, Gamma, Iota, were assumed to be 50%, 60%, 35% higher than the original strain, and the transmissibility of Delta was assumed to be 30% higher than Alpha.⁸⁻¹³

Disease dynamics

The infectivity of asymptomatic, mild symptomatic, and severe symptomatic states was set to 26%, 44%, and 89% relative to the pre-symptomatic stage.¹⁴⁻¹⁶ The incubation period was sampled from a log-normal distribution with a mean of 5.2 days.¹⁷ An age-dependent proportion of infected individuals progressed to a pre-symptomatic stage¹⁸ with a mean duration of 2.3 days, sampled from a Gamma distribution.^{15,19} Pre-symptomatic cases developed symptomatic disease with an average infectious period of 3.2 days, which was also sampled from a Gamma distribution.^{20,21} Infected individuals who remained asymptomatic had an average infectious period of 5 days sampled from a Gamma distribution.^{20,21}

Based on the reduced neutralizing activity of convalescent sera against Gamma and Delta,²²⁻²⁵ we assumed that these variants evade naturally acquired immunity by an average of 21% (95% CI: 11-36%).^{26,27} This evasion rate was implemented as a reduction of immune protection for

individuals recovered from the original strain or the Alpha variant, corresponding to per-contact transmission probability of 0.0223 and 0.014 in Florida and Texas. We further assumed that recovery from infection due to the Gamma or Delta variant provides protection against all variants in the model, preventing reinfection for at least one year.

Infection outcomes

We assumed that asymptomatic and mild symptomatic cases recover from infection without hospitalization. Severely ill cases were hospitalized within 2-5 days of symptom onset^{28,29} and were therefore removed from the transmission chain. All symptomatic cases who were not hospitalized were assumed to self-isolate within 24 hours of symptom onset, reducing their number of daily contacts by an average of 74% (Table S1). Intensive care unit (ICU) and non-ICU hospitalization rates were parameterized (Table S2) by clinical and epidemiological data stratified by age and comorbidities.³⁰⁻³² Infection with Alpha and Delta variants was associated with 30% higher risk of death,^{9,10} and infections with the Gamma variant were assigned the case fatality of the original strain. The risk of hospitalization with the Delta variant was assumed to be 2.26 times higher than that due to infection with Alpha.³³

Table A2. Model parameters associated with hospitalization of severe cases.

Proportion of severe cases hospitalized with one or more comorbidities	100%	30-32
Non-ICU	60.4%	
ICU	39.6%	
Proportion of severe cases hospitalized without any comorbidities	10.8%	30-32
Non-ICU	75%	
ICU	25%	
Length of non-ICU stay (days)	Gamma(shape: 4.5, scale: 2.75)	Derived from 34,35
Length of ICU stay (days)	Gamma(shape: 4.5, scale: 2.75) + 2	Derived from 34,35

Vaccination

We implemented a two-dose vaccination campaign with a sequential prioritization of (i) healthcare workers (5% of the total population)³⁶, adults with comorbidities, and those aged 65 and older; and (ii) other individuals aged 16-64^{37,38}. Daily vaccination rates were implemented based on the number of vaccine doses administered in different age groups^{39,40}. The minimum

age-eligibility for vaccination was 16 years before May 13, 2021 after which children aged 12 to 15 years became eligible for vaccination.

The time interval between first and second doses of Pfizer-BioNTech and Moderna vaccines were specified to be 21 and 28 days, respectively. ^{41,42} The model was parameterized with published estimates of vaccine efficacy following each dose of Pfizer-BioNTech and Moderna vaccines against infection, symptomatic disease, and severe disease ⁴³⁻⁴⁶ (Table S3). These efficacies were implemented in the model as a reduction of transmission probability (for efficacy against infection), reduction in the probability of developing symptomatic disease, and reduction of severe illness if symptomatic disease occurred.

For the counterfactual scenario of achieving 74% vaccination coverage of adults by July 31, 2021 in Florida and Texas, we increased the daily vaccine doses in the model by 32% and 35%. The additional vaccines were distributed to individuals aged 18 and older in the same priority as described above.

Table A3. Estimated vaccine efficacies (%) from published studies.

Vaccine efficacy	Weeks after the first dose		Weeks after the second dose		Reference
	1-2	3	1-2	>2	
Original strain/Iota	1-2	3	1-2	>2	42,45,47-50
Infection	None	46 (40, 51)	60 (53, 66)	86.1% (82.4, 89.1)	
Symptomatic disease	None	57 (50, 63)	66 (57, 73)	94 (87, 98)	
Severe disease	None	62 (39, 80)	80 (59, 94)	92 (75, 100)	
Alpha variant	1-2	3	1-2	>2	46,51,52
Infection	None	29.5 (22.9, 35.5)	60 (53, 66)	89.5 (85.9, 92.3)	
Symptomatic disease	None	53.6 (50, 63)	62 (57, 73)	93.7 (91.6, 95.3)	
Severe disease	None	54.1 (26.1, 71.9)	80 (59, 94)	94 (87, 98)	
Gamma variant *	1-2	3	1-2	>2	46,51
Infection	None	36.8 (32., 40.8)	48 (42.4, 52)	73.6 (70.4, 76)	
Symptomatic disease	None	33.2 (8.3, 51.4)	66 (57, 73)	94 (87, 98)	

Severe disease	None	34 (0, 50)	68 (64, 75)	97.4 (92.2, 99.5)	51,53,54
Delta variant	1-2	3	1-2	>2	
Infection	None	36.8 (32., 40.8)	48 (42.4, 52)	64 (57, 70)	
Symptomatic disease	None	33.5 (20.6, 44.3)	62 (57, 73)	88 (85.3, 90.1)	
Severe disease	None	34 (0, 50)	68 (64, 75)	93 (89, 97)	

* Vaccine efficacy against the Gamma variant was assumed to be the same as those reported for Beta.

Model implementation

We simulated the model with a population of 100,000 individuals for each state from October 1, 2020 to July 31, 2021. This population is a scalable size in agent-based modelling and is considered sufficiently large to capture the heterogeneity. At the start of simulations, we considered pre-existing immunity levels of 5.7% and 5.8% in Florida and Texas, respectively.⁵⁵ Vaccination was initiated on December 12, 2020, and rolled out as a two-dose strategy. On April 2, the guidelines by the US Centers for Disease Control and Prevention indicated a minimal risk for fully vaccinated individuals to return to pre-pandemic normal activities ⁵⁶. We therefore allowed vaccinated individuals to return to their normal contact pattern behaviour 14 days after the second dose of vaccine from April 3, 2021. The simulations were performed using a daily time-step and the model timelines correspond to the period of October 1, 2020 to October 31, 2021. The results were averaged over 500 independent Monte-Carlo realizations, which were sufficient for stabilization. The model was implemented in Julia, and simulation codes are available at: https://github.com/thomasvilches/multiple_strains/tree/TXnFL

Simulation results

We further projected the epidemiological impact of a 50% increase in the daily vaccination rate compared to the status quo in the two states, starting from September 1, 2021 (Orange curves in Figure 1 and Figures A1-A2). While limited in short term-impact, this boosting of vaccination would still prevent an estimated additional 26,690 cases, 4,654 hospitalizations, and save 1,424 more lives in Florida by the end of October 2021. The same increase in Texas vaccination program would avert additional 35,357 cases, 1,873 hospitalizations and 1,268 deaths.

For both counterfactuals scenarios of 74% vaccination coverage (by July 31, 2021) and 50% increase in the daily vaccination rate (starting from September 1, 2021), we performed Kruskal–Wallis (one-way ANOVA) tests to determine the significance in reduction of cases, hospitalizations and deaths at a 5% significance level. For the first counterfactual, the null hypothesis was rejected (p-value<0.0001) for all measures in Florida and Texas, and thus the distributions of the total number of infections, hospitalizations, and deaths were significantly different from the observed data. For the second counterfactual scenario, the Kruskal–Wallis

test did not reject the null hypothesis that all simulated data samples come from the same distributions ($p\text{-value} > 0.25$).

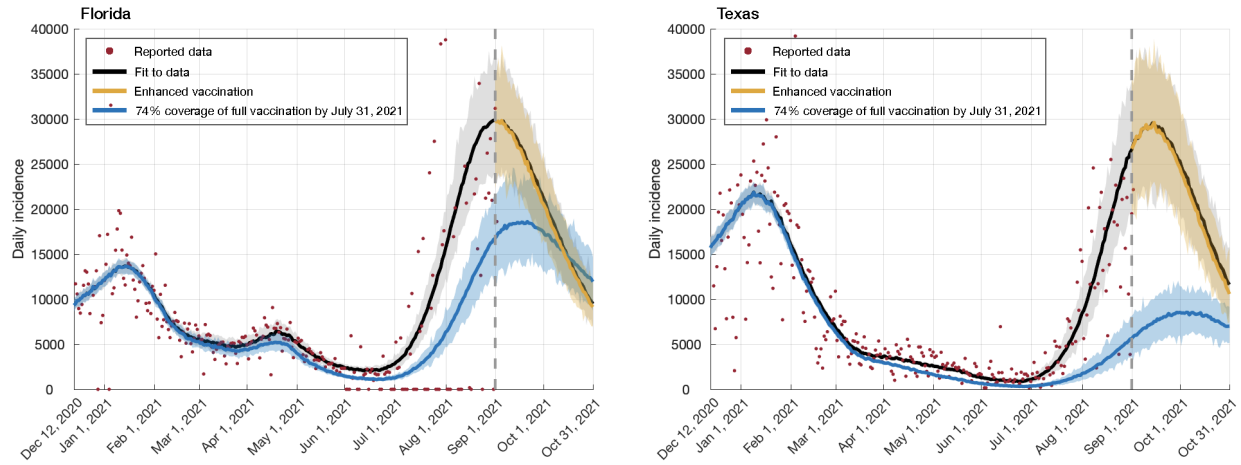


Figure A1: Model fit to daily incidence of infections in Florida and Texas (mean estimates: black curves) with uncertainty bounds of simulations represented in grey shaded areas. Red dots are reported incidence. Blue curves (mean estimates) and shaded areas show the model projections of daily incidence under the counterfactual scenario of enhanced vaccination with 74% coverage of adults by July 31, 2021. The orange curves (mean estimates) and shaded areas represent the model projections for the scenario of 50% increase in daily vaccination rate starting from September 1, 2021.

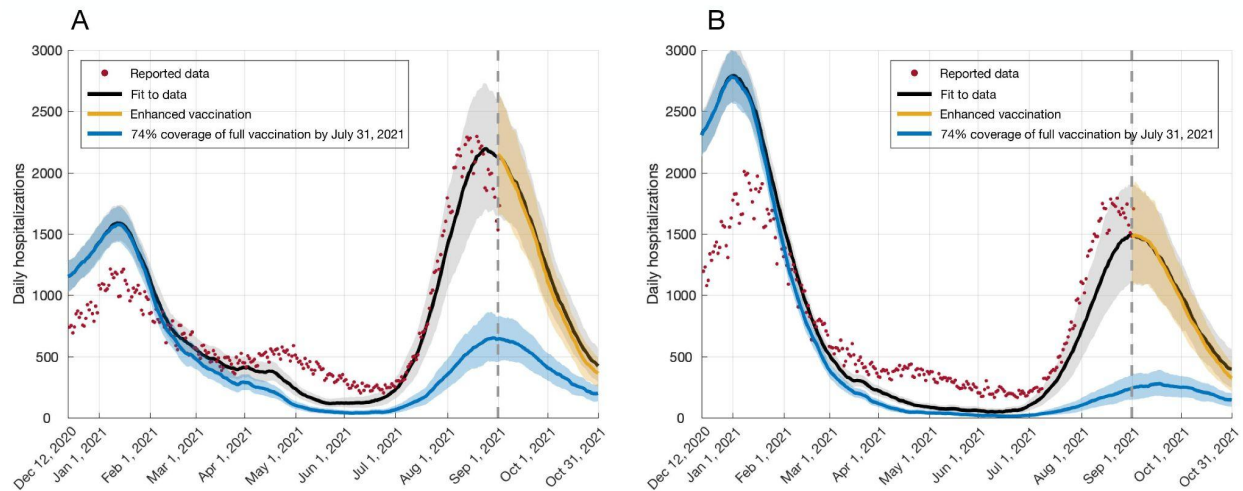


Figure A2: Model projections of daily hospitalizations in (A) Florida and (B) Texas (mean estimates: black curves) with uncertainty bounds of simulations represented in grey shaded areas. Red dots are reported data. Blue curves (mean estimates) and shaded areas show the model projections under the counterfactual scenario of enhanced vaccination with 74% coverage of adults by July 31, 2021. The orange curves (mean estimates) and shaded areas

represent the model projections for the scenario of 50% increase in daily vaccination rate starting from September 1, 2021.

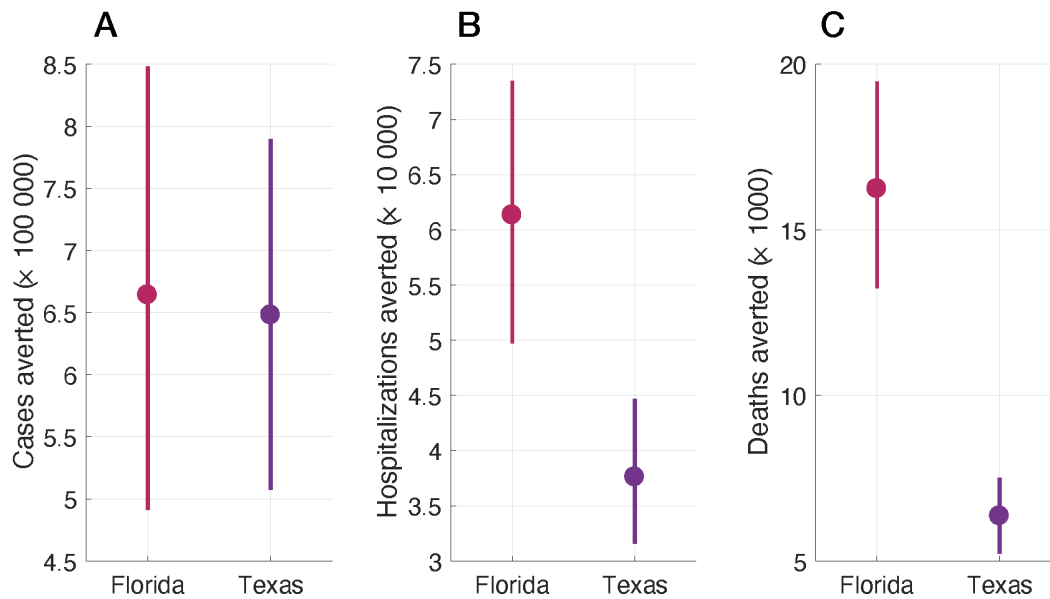


Figure A3: Estimated cases (A), hospitalizations (B), and deaths (C) that would have been averted in Florida and Texas between December 12, 2020 and August 31, 2021 if vaccination coverage of adults had reached 74% by July 31, 2021.

Comparisons with previous work

Few studies have also attempted to project the epidemiological impact of non-pharmacologic measures and vaccination in Florida and Texas.⁵⁷⁻⁵⁹ For example, a study calibrated to outbreak data in Florida prior to vaccine rollout, projected that a highly effective vaccine could avert more than 2 million infections and 55,000 deaths under 75% vaccine coverage.⁵⁹ This study, however, was conducted before vaccine rollout and did not account for transmission dynamics of SARS-CoV-2 variants. Other studies have projected the expected number of cases,⁶⁰ hospitalizations and ICU admissions⁶¹ under status-quo vaccination rates. To our knowledge, the impact of a counterfactual scenario of boosted vaccination in Florida and Texas taking into account the transmission dynamics of SARS-CoV-2 variants and actual vaccine rollout data has not been investigated.

Limitation

For the impact of enhanced vaccination programs, we note that our simulations are subject to some limitations. We considered vaccine distributions and the efficacy data of the Pfizer-BioNTech and Moderna vaccines. Combined, these two vaccines constitute ~96% of doses administered in the United States. A third single-dose vaccine developed by Johnson and Johnson is also authorized for emergency use in the United States, which has a slightly lower efficacy compared to the Pfizer-BioNTech and Moderna vaccines.^{62,63} Considering the lower efficacy of Johnson and Johnson in preventing infection, symptomatic and severe disease, our results might be subject to an overestimate of vaccination impact in reducing COVID-19 burden.

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