Population immunity to pre-Omicron and Omicron SARS-CoV-2 variants in US states and counties through December 1, 2021

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Running title: Immunity to SARS-CoV-2 in the US

Abstract

Background: Both SARS-CoV-2 infection and COVID-19 vaccination contribute to population-level immunity against SARS-CoV-2. This study estimates the immunological exposure and effective protection against future SARS-CoV-2 infection in each US state and county over 2020-2021, and how this changed with the introduction of the Omicron variant.

Methods: We used a Bayesian model to synthesize estimates of daily SARS-CoV-2 infections, vaccination data and estimates of the relative rates of vaccination conditional on infection status to estimate the fraction of the population with (i) immunological exposure to SARS-CoV-2 (ever infected with SARS-CoV-2 and/or received one or more doses of a COVID-19 vaccine), (ii) effective protection against infection, and (iii) effective protection against severe disease, for each US state and county from January 1, 2020, to December 1, 2021.

Results: The estimated percentage of the US population with a history of SARS-CoV-2 infection or vaccination as of December 1, 2021, was 88.2% (95% Credible Interval (CrI): 83.6%-93.5%). Accounting for waning and immune escape, effective protection against the Omicron variant on December 1, 2021, was 21.8% (95%CrI: 20.7%-23.4%) nationally and ranged between 14.4% (95%CrI: 13.2%-15.8%, West Virginia) to 26.4% (95%CrI: 25.3%-27.8%, Colorado). Effective protection against severe disease from Omicron was 61.2% (95%CrI: 59.1%-64.0%) nationally and ranged between 53.0% (95%CrI: 47.3%-60.0%, Vermont) and 65.8% (95%CrI: 64.9%-66.7%, Colorado).

Conclusions: While over four-fifths of the US population had prior immunological exposure to SARS-CoV-2 via vaccination or infection on December 1, 2021, only a fifth of the population was estimated to have effective protection against infection with the immune-evading Omicron variant.

Keywords: SARS-CoV-2; immunological exposure; effective protection

Introduction

By December 1, 2021, over 48 million COVID-19 cases and 780,000 COVID-19-associated deaths had been reported in the United States[1,2]. Between December 1, 2021, and February 1, 2022, an additional 26 million cases (35% of cumulative US COVID-19 cases) and 100,000 deaths (11% of all US COVID-19 deaths) were reported[3]. Reducing COVID-19 morbidity and mortality depends largely on reaching high levels of population immunity. The emergence of the Omicron variant[4,5] illustrates the importance of identifying areas of highest vulnerability, and underscores how continued viral evolution may reduce effective protection.

The true number of SARS-CoV-2 infections that have occurred is unknown. Recent estimates of the percentage of the US population ever infected vary between 37% and 62%[6-9]. Seroprevalence estimates from a nationwide convenience sample suggested that as of December 21, 2021, 33.5% of the US population over 16 years old had infection-induced SARS-CoV-2 antibodies[10]; a nationwide blood-donor study estimated 28.8% infection-induced seroprevalence for the same period[11]. The level of protection that infection confers, and the rate at which protection and seropositivity wane, are incompletely understood[12-14].

By December 1, 2021, over 240 million US residents (72.9%) had received at least one dose of a COVID-19 vaccine[1], and over 80 million residents had received both the initial one- or two-dose schedule and a booster. Reported efficacy against symptomatic infection for the three vaccines available in the US ranged from 66% (Johnson & Johnson) to 94% (Pfizer and Moderna) in clinical trials[15-17]. Vaccine efficacy against infection was estimated to be lower during the Delta surge compared to earlier waves, and further reductions in efficacy against the Omicron variant have been reported[4,5]. Declines in vaccine efficacy may reflect both waning immunity and increased immune escape for viral variants. Despite evidence of waning efficacy[18-21], vaccination appears to provide durable protection against severe disease, and boosters partially restore vaccine efficacy.[22-24]

Local estimates of population immunity are important for understanding the risks of continued SARS-CoV-2 transmission. State-level estimates of infection- and vaccine-induced SARS-CoV-2 seroprevalence based on blood donation data have been reported[25], with estimates for May 2021 ranging from 63.7% in Mississippi to 91.7% in Connecticut. While these estimates provide a direct measure of seroprevalence in the study populations, they may be affected by systematic differences between blood donors and the general population. Moreover, these data do not provide county-level estimates or account for waning of protection.

For this study, we used state- and county-level modeled estimates of cumulative SARS-CoV-2 infections and reported coverage for initial and booster vaccination[6,26]. We estimated the joint distribution of prior SARS-CoV-2 infection and vaccination from survey data[27]. Using these inputs in a Bayesian analytic framework, we estimated the population with SARS-CoV-2 immunological exposure (ever infected or vaccinated) for each US state and county through December 1, 2021. Incorporating evidence on the time-course of natural and vaccine-induced immunity, we estimated effective population immunity against infection and against severe disease over time, as well as effective protection against the Omicron variant, accounting for immune escape.

Methods

Data

Infections

We extracted time-series estimates of SARS-CoV-2 infections from a statistical model[6] that synthesizes reported data on COVID-19 cases and deaths[3,28], accounting for both under-ascertainment and time lags. We imputed missing cases and deaths data for Nebraska counties after June 30, 2021 (see SI Methods).

We estimated cumulative infections for each US state and 3137 counties from the first reported case date until December 1, 2021. Across all states and counties, dates for the first reported case ranged between December 16, 2019 and November 12, 2020 (interquartile range: February 20-March 7, 2020). We excluded 6 counties due to missing/insufficient data.

Vaccinations

We extracted estimates from a repository reporting weekly county-level vaccination coverage based on CDC-reported data, adjusted for known biases and incompleteness in several states[29,30]. We imputed missing data and smoothed the weekly time-series[31] into a daily time-series of residents having received at least one vaccine dose (see SI Methods). We summed these counts for all counties within each state to produce state-level estimates. We extracted daily state- and county-level booster coverage data from CDC reports[26]. County-level booster coverage reporting started on December 16, 2021. Booster coverages before this date were imputed proportional to the corresponding state coverage using the ratio of county to state booster coverage on December 16, 2021.

Co-occurrence of infection and vaccination

The Census Bureau's Household Pulse Survey collects data on COVID-19-relevant beliefs and behaviors at two-weekly intervals, for individuals 18 years and older[27]. We extracted data from February 2 to August 30, 2021, to estimate the joint distribution of infection and vaccination among survey respondents. We extracted the variables *had covid* (Yes/No; whether a respondent has received a positive COVID-19 diagnosis), *received vaccine* (Yes/No; whether a respondent has received as least one dose of a COVID-19 vaccine), *state* and *week*. Responses other than Yes or No (e.g., Unknown) were excluded (2.3% of respondents).

Estimation

For each location, we computed the percentage *immunologically exposed*, defined as the percentage of the population with a prior SARS-CoV-2 infection, at least one dose of a COVID-19 vaccine, or both. We calculated values separately for individuals aged less than 12 years and those 12 years or older, due to differences in vaccine eligibility for these groups over the study period.

Immunological exposure for the population aged 12 and over

Using the Household Pulse data, we fit a logistic regression model to estimate the association between self-reported vaccination status and prior COVID-19 diagnosis. We operationalized this relationship as the odds ratio for reported vaccination, comparing individuals reporting a prior

COVID-19 diagnosis to those reporting no prior diagnosis (see SI Methods). Using these regression results, we created state-specific prior distributions for the odds ratio of vaccination given prior infection status, for individuals aged 12 and older (Table S1). This approach assumes that the odds ratio for vaccination among those with a prior undiagnosed infection is the same as for those with a prior diagnosed infection. We validated this relationship using data from the Axios-Ipsos Coronavirus Tracker[32].

We calculated the joint probability of being vaccinated or infected as the sum of the marginal probabilities for prior infection and prior vaccination, minus the probability of being both infected and vaccinated, to avoid double counting (see SI Methods).

Immunological exposure for the population under 12 years old

For the population under 12 years old, the percentage *immunologically exposed* was assumed equal to the estimated percentage ever infected, as this age group was not eligible for vaccination during most of the study period. We assumed infection prevalence in this age group was equal to prevalence in the overall population. We combined under-12 and over-12 immunity estimates in a weighted sum to obtain the percentage *immunologically exposed* in the full population. We validated our results by comparing to published population immunity estimates based on laboratory data from a blood-donor sample[25].

Waning of protection

Protection conferred by natural infection and vaccination declines over time[24,33-35]. Recent studies suggest antibody titers decay rapidly in the three months following infection and more gradually thereafter[14,36]. Neutralizing antibody activity has been observed up to eight months after symptom onset[12], and simulation studies suggest that titers wane below 1:20 (often used to infer 50% protection) for the majority of previously-infected individuals by 341 days after symptom onset[14]. Antibody titers in vaccinated individuals are believed to wane at similar rates[13], although vaccine efficacy against symptomatic SARS-CoV-2 infection has been shown to remain robust in the first six months following inoculation[20,21]. Based on studies of antibody titers, clinical trials and vaccine effectiveness studies, we formulated three simplified waning scenarios, designed to capture major uncertainties in waning rates (Figure S1). For the main analysis (base-case scenario), we assumed that infection or vaccination each initially confer 80% protection against infection that declines to 25% by 12 months after exposure, and protection against severe disease starts at 95% and declines to 85% after 12 months. For individuals both infected and vaccinated, we assumed constant protection of 90% against infection and 95% against severe disease. See SI Methods for optimistic and pessimistic scenarios used in sensitivity analyses. We assumed that booster uptake was randomly distributed in the eligible (fully vaccinated) population, and that receiving a booster restored immunity to original (pre-waning) levels and subsequently waned following the 'both infected and vaccinated' curve[23,24,37].

Immune escape under the Omicron variant

Early evidence indicates the Omicron variant can escape immunity acquired by immunization or infection with earlier variants[4,38]. Available evidence suggests the immune escape may range between a thirty-fold drop[38] to halving of the protection of earlier variants, with greater protection retained by boosted individuals[22].. Protection against severe disease appears more robust[39]. We translated this evidence into *high*, *medium* (used in the main analysis) and *low* immune-escape scenarios, to capture a simplified yet plausible range of scenarios. In the *medium* escape scenario, protection against infection was reduced by 70% (40% for those who received a booster) and protection against severe disease was reduced by 20% (15% for those who received a booster) compared to immunity against pre-Omicron variants. See Table S2 for *low* and *high* escape scenarios.

Model implementation

We executed the analysis in R[40] and the rstan package[41] (https://github.com/covidestim/covidestim/tree/immunity-waning). For state-level results, we report uncertainty using equal-tailed 95% credible intervals (95%CrI). We calculated national estimates and conservative uncertainty intervals by summing state-level estimates and upper and lower bounds of state-level intervals. County-level estimates were produced using an optimization routine[6] that produces point estimates without uncertainty intervals. In summarizing county-level results, we excluded counties with a population under 1,000 (0.9% of all counties).

Results

By December 1, 2021, 59.2% (95% Credible Interval (CrI): 46.9%—75.6%) of the US population was estimated to have been infected with SARS-CoV-2, with state-level estimates ranging from 24.0% (95%CrI: 16.0%—40.3%, Hawaii) to 78.5% (95%CrI: 68.7%—88.6%, New Mexico). County-level estimates ranged from 9.0% (San Juan County, Washington) to 91.3% (San Juan County, New Mexico). The percentage of the US population that received at least one COVID-19 vaccine dose was estimated to be 65.2%. State-level coverage varied between 32.0% (West Virginia) and 82.8% (New Hampshire) and county-level coverage varied between 13.3% (Morgan County, West Virginia) and 89.9% (Pitkin County, Colorado).

Based on the results of the Household Pulse Survey, individuals reporting a prior COVID-19 diagnosis were substantially less likely to report being vaccinated. The odds ratio of vaccination among individuals with a prior COVID-19 diagnosis (compared to no prior diagnosis) varied from 0.40 (95%CrI: 0.36–0.44) in Florida to 0.58 (95%CrI: 0.53—0.63) in Texas, with a national mean of 0.52 (95%CrI: 0.50—0.55).

Immunological exposure

The national estimate for the population *immunologically exposed* was 88.2% (95%CrI: 83.6%—93.5%). State-level estimates ranged from 76.9% (95%CrI: 67.6%—87.6%, West Virginia) to 94.4% (95%CrI: 91.2%—97.3%, New Mexico; Table 1). Across counties, the percentage *immunologically exposed* ranged from 42.4% (Sioux County, Nebraska) to 98.3% (San Juan County, New Mexico; interquartile range 80.2—87.3%; Figure 1, Figure S2).

Effective protection

Accounting for waning of immunity, the percentage of the US population with *effective protection* against infection with pre-Omicron variants increased from 14.7% (95%CrI: 11.1%—19.8%) on January 1, 2021, to 54.1% (95%CrI: 50.5%—59.2%) by December 1, 2021. On December 1, 2021, *effective protection* against infection with the Omicron variant was estimated to be 21.8% (95%CrI: 20.7%—23.4%). The percentage of the population with *effective protection* against severe disease was estimated to be 74.1% (95%CrI: 71.4%—77.6%) for pre-Omicron variants and 61.2% (95%CrI: 59.1%—64.0%) for the Omicron variant.

Effective protection against infection with Omicron varied across states between 14.4% (95%CrI: 13.2%—15.8%, West Virginia) and 26.4% (95%CrI: 25.3%—27.8%, Colorado). *Effective protection* against severe disease ranged between 53.0% (95%Cri: 47.3%—60.0%, West Virginia) and 65.8% (95%CrI: 64.9%—66.7%, Colorado) (Table 1).

Figure 2 shows how state-level percentages *immunologically exposed*, *effectively protected* against infection, and *effectively protected* against severe disease have have evolved over the course of the epidemic and with the introduction of Omicron. For counties, the percentage of the population with *effective protection* against infection and severe disease caused by pre-Omicron variants, respectively, varied between 26.6% and 48.4% (Cameron Parish, Louisiana) and 72.5% and 77.4% (Fairfax City, Virginia; Figure 3). Estimates of *effective protection* against infection and severe disease, respectively, from the Omicron variant varied between 8.4% and 26.4% (McPherson County, Nebraska), and 33.1% and 71.3% (Mineral County, Colorado; Figure S3).

Relative contributions of prior infection and vaccination

On December 1, 2021, 23.0% (95%CrI: 18.4%—28.3%) of the US population was estimated to have been infected but not vaccinated, 29.0% (95%CrI: 18.0%—36.8%) was estimated to have been vaccinated but not infected, and 36.2% (95%CrI: 28.4%—47.2%) was estimated to have been both vaccinated and infected. Relative contributions of vaccination and prior infection varied widely across states and counties and over time (Figures S4 and S5). Figure 4 highlights regional patterns in the different pathways to overall immunity on December 1, 2021. The state-population weighted regional averages of the population *immunologically exposed* were 89.1% in the West (20.4% only infected, 30.8% only vaccinated), 84.7% in the Midwest (24.8% only infected, 30.0% only vaccinated), 88.3% in the South (27.5% only infected, 24.4% only vaccinated), and 91.0% in the Northeast (14.5% only infected, 35.5% only vaccinated).

Validation

We re-estimated the odds ratio of vaccination given prior infection using independent survey data, allowing bi-weekly national estimates between January and June 2021[42] (SI Methods). For the 13 survey waves included in this period, the odds ratio of vaccination given prior infection varied between 0.35 and 0.98, and the mean odds ratio was 0.51 (95%CrI: 0.44—0.59), similar to the estimated national value in the main analysis. We compared our estimates of the percentage of the population *immunologically exposed* with blood donor seroprevalence estimates (Figure S6). Our estimates of the percentage *immunologically exposed* were generally lower than seroprevalence estimates from Jones et al.[25]

Sensitivity analyses

We conducted additional analyses evaluating the sensitivity of our *effectively protected* estimates to waning assumptions, with pessimistic and optimistic scenarios (SI Methods and Figures S1), in combination with the Omicron immune-escape scenarios (Table S2). In these analyses, national estimates of *effective protection* against infection from pre-Omicron variants ranged between 47.1% and 64.3%, and protection against infection with Omicron ranged between 12.3% and 28.4% (Table S3). *Effective protection* against severe disease from pre-Omicron variants ranged between 67.5% and 79.0%, and protection against severe disease from the Omicron variant ranged between 57.4% and 61.7% (Table S4).

Discussion

We analyzed the joint distribution of COVID-19 vaccination and prior SARS-CoV-2 infection in each US state and county since the beginning of the COVID-19 epidemic and estimated how population immunity changed over this period. By December 1, 2021, over three-quarters of the US population had prior immunological exposure to SARS-CoV-2 via vaccination or infection; half of the population retained *effective protection* against infection with previously circulating variants, while only a fifth of the population had *effective protection* against infection with the Omicron variant.

This study has several limitations. Firstly, we chose to model the under 12 and over 12 populations separately. On November 1, 2021, children 5-11 years old became eligible for vaccination; however, we did not account explicitly for the initial vaccination scale-up through December 1, 2021, in this group. For other ages, we used vaccination coverage data from Merritt *et al*[29,30], which endeavors to address known biases in CDC vaccination data. We further adjusted these data to assure that no greater than 100% of the over 12 population could have been vaccinated by the end of our study period. Furthermore, we assumed the cumulative infections to be proportional between the under 12 and over 12 populations. While some indicators suggest lower cumulative infections among children, other evidence shows the opposite pattern, with that contradicts this and suggests a higher seroprevalence for children compared to adults[43-46].

Secondly, to estimate *effective protection*, we made assumptions about how natural and vaccine-induced immunity wanes over time. Despite accumulating evidence, these assumptions are still uncertain. In sensitivity analyses, we examined additional waning scenarios, providing a range of plausible values for the level of *effective protection*. We did not account for differences in waning for the pre-Omicron SARS-CoV-2 variants. Our assumptions regarding the immune escape of the Omicron variant are preliminary. The presented range of plausible scenarios demonstrates that SARS-CoV-2 variants that evade immune protection may spread widely despite high prevalence of prior infection and vaccine coverage.

Thirdly, the model for infections assumes individuals can only be infected once, so possible reinfections and breakthrough infections amongst vaccinated individuals are not accounted for in our estimates of immunity. For this reason, and because reinfections and breakthrough infections with Omicron are common, we only used estimates of infections up until December 1, 2021.

Fourthly, we estimated the relationship between prior infection and vaccination status using survey data that have been criticized for non-representativeness[32]. While this relationship was confirmed in independent survey data validated against external benchmarks[32], it is still possible that reporting biases could have distorted this relationship. If there is greater overlap between vaccinated and previously infected populations, then overall population immunity will be lower than estimated in our analyses. Finally, we assumed that booster uptake was randomly distributed among the eligible (vaccinated) population.

Existing and new SARS-CoV-2 variants will likely continue circulating, since neither natural infection nor offers permanent immunity against infection. Recent CDC recommendations for local COVID-19 monitoring focus on hospitalizations per capita[47]. However, monitoring community outbreaks through signals such as testing volume and surveillance of wastewater data remains important[48,49]. Estimates of effective protection against infection and severe disease in the population presented in this study provide valuable insight into assessing the local risk of counties and states in the US.

Conclusions

As of December 1, 2021, the fraction of the US population that had ever been infected with SARS-CoV-2 and/or received at least one dose of a COVID-19 vaccine varied between counties and states. Accounting for waning of population immunity, *effective protection* against infection by pre-Omicron variants in US states was between 27.6% and 40.4% lower than the percentage *immunologically exposed.* Introduction and takeover of the Omicron variant reduced *effective protection* against infection by another 26.2% to 37.0% across US states.

NOTES

Author contributions: TC, NAM and JAS conceived and supervised the project. TC, NAM and JAS acquired funding. FK wrote the model code, drafted the original manuscript and visualized the results. FK and MR curated the data and executed the analysis. All authors contributed to the development of the methodology, and reviewed and edited the original manuscript.

Disclaimer: The findings, conclusions, and views expressed are those of the author(s) and do not necessarily represent the official position of the Centers for Disease Control and Prevention (CDC), Council of State and Territorial Epidemiologists (CSTE), or National Institutes of Health (NIH). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Funding

This project has been funded (in part) by contract 200-2016-91779 with the Centers for Disease Control and Prevention.

VEP reports grants from National Institute of Allergy and Infectious Diseases R01 AI137093

TC reports grants from National Institute of Allergy and Infectious Diseases R01 AI112438 and the Centers for Disease Control and Prevention though the Council of State and Territorial Epidemiologists (NU38OT000297-03)

NAM reports grants from National Institute of Allergy and Infectious Diseases R01 AI146555-01A1, the Centers for Disease Control and Prevention though the Council of State and Territorial Epidemiologists (NU38OT000297-03), and the Centers for Disease Control and Prevention (75D30121F0003).

JAS reports funding from the Centers for Disease Control and Prevention though the Council of State and Territorial Epidemiologists (NU38OT000297-02) and the National Institute on Drug Abuse (3R37DA01561217S1).

FK reports support for this work from Centers for Disease Control and Prevention, National Institute of Allergy and Infectious Diseases, and Council of State and Territorial Epidemiologists, all paid to institution.

NAS reports support for this work from Council of State and Territorial Epidemiologists.

Conflicts of interest:

VEP reports grants to her institution, unrelated to this work, from Bill & Melinda Gates Foundation, US Centers for Disease Control and Prevention, Gavi, the Vaccine Alliance, and NIH/NIAID, is an unpaid member of WHO IVIR-AC and has received reimbursement from Merck and Pfizer for travel expenses to Scientific Input Engagements unrelated to the topic of this manuscript (<\$500). MHC reports support for attending meetings and/or travel from WHO Global Task Force on TB Impact Measurement. NAS reports grants or contracts unrelated to this work from Centers for Disease Control and Prevention and National Institutes of Health. NAM reports grants or contracts to institution and unrelated to this work from Bill and Melinda Gates Foundation, The European Commission, World Health Organization, and USAID; consulting fees paid to author from World Health Organization and Global Fund to Fight AIDS TB and Malaria; support for attending meetings and/or travel from Bill and Melinda Gates Foundation. All other authors have declared that no competing interest exist.

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Table 1: Key population immunity outcomes for each US state on December 1, 2021.

State	Percentage ever vaccinated*	Percentage ever infected (95%CrI)	Ratio percentage vaccinated / percentage infected	Percentage *immunologically exposed* (95%CrI)	Percentage *effectively protected* against infection, pre-Omicron variants (95%CrI) **	Percentage *effectively protected* against severe disease, pre-Omicron variants (95%CrI) **	Percentage *effectively protected* against infection with Omicron (95%CrI)***	Percentage *effectively protected* against severe disease from Omicron (95%CrI)***
Alabama	52.4%	71.3% (60%-84.2%)	0.73	88.6% (83%-94.3%)	52.8% (50%-55.9%)	74.1% (70.3%-78.2%)	20.7% (19.9%-21.7%)	61% (57.9%-64.3%)
Alaska	58.3%	66.8% (54.8%-81.2%)	0.87	88.7% (83.3%-94.2%)	57.7% (54.2%-61.4%)	73.9% (70.4%-77.9%)	24.2% (23.2%-25.4%)	61.6% (58.8%-64.8%)
Arizona	62.5%	77.6% (67.6%-88.1%)	0.81	93.4% (89.7%-96.8%)	58.8% (56.1%-61.5%)	77.3% (75%-79.5%)	22.9% (22.1%-23.8%)	63.7% (61.9%-65.5%)
Arkansas	52.8%	64.3% (52%-79.4%)	0.82	85.8% (79.5%-92.6%)	50.5% (47.4%-54.5%)	71.5% (67.3%-76.3%)	20.6% (19.8%-21.9%)	59.1% (55.8%-63%)
California	71.4%	57.2% (44.5%-74.1%)	1.25	89.4% (85.6%-93.9%)	55.3% (51.3%-60.8%)	75.3% (73.4%-77.9%)	22.1% (20.9%-23.8%)	62.2% (60.7%-64.3%)
Colorado	79.1%	63.7% (51.4%-79%)	1.24	93.3% (90.6%-96.3%)	63.2% (59.6%-67.8%)	78.9% (77.9%-80.1%)	26.4% (25.3%-27.8%)	65.8% (64.9%-66.7%)
Connecticut	82.3%	48.4% (36.1%-66.7%)	1.7	91.6% (89.2%-94.8%)	58.8% (54.9%-64.8%)	79.5% (78.7%-80.7%)	24.1% (23%-25.9%)	65.9% (65.3%-66.8%)
Delaware	69.4%	60.3% (47.8%-76.5%)	1.15	89.8% (85.6%-94.5%)	56.8% (53.2%-61.7%)	75.8% (73.5%-78.6%)	23.2% (22.2%-24.7%)	62.8% (61%-65.1%)
District of Columbia	78.3%	48.8% (36.5%-67.1%)	1.6	90.0% (86.9%-94%)	55.7% (51.8%-61.8%)	77.3% (76.2%-79.1%)	21.2% (20%-23%)	63.4% (62.5%-64.8%)
Florida	70.7%	69% (57.3%-82.6%)	1.03	93.2% (90%-96.4%)	60.5% (56.7%-64.8%)	78.5% (76.5%-80.7%)	23.5% (22.3%-24.8%)	64.7% (63%-66.5%)
Georgia	50.8%	71.2% (59.9%-84.1%)	0.71	88.4% (82.8%-94.1%)	51.8% (48.7%-55.1%)	73.4% (69.5%-77.6%)	20.2% (19.2%-21.2%)	60.3% (57.2%-63.7%)
Hawaii	82.1%	24% (16%-40.3%)	3.43	86.8% (85.2%-90%)	46.4% (43.5%-52.6%)	77.3% (76.9%-78.3%)	17.8% (16.9%-19.6%)	63.2% (62.9%-64%)
Idaho	49.4%	68.6% (56.9%-	0.72	86.8% (80.4%-93.4%)	54.7% (51.7%-	72.5% (68.1%-	23.4% (22.6%-	60.4% (57%-64.3%)

		82.4%)			57.5%)	77.3%)	24.3%)	
Illinois	68.3%	52.4% (39.9%-70.2%)	1.3	87.2% (82.9%-92.6%)	52.6% (48.9%-58.1%)	73.3% (71%-76.6%)	22.2% (21.1%-23.9%)	60.9% (59.1%-63.5%)
Indiana	54.9%	55.2% (42.6%-72.5%)	1	82.9% (76.6%-90.4%)	47.9% (44.4%-53%)	68.8% (64.9%-74.2%)	19.8% (18.8%-21.4%)	57% (53.8%-61.3%)
Iowa	60.8%	56.4% (43.8%-73.5%)	1.08	85.3% (79.7%-91.9%)	53% (50%-57.3%)	71.4% (68.2%-75.7%)	23.9% (23.1%-25.2%)	60% (57.4%-63.4%)
Kansas	61.4%	59.3% (46.7%-75.7%)	1.04	86.8% (81.4%-92.8%)	52.6% (49.2%-57.2%)	72.3% (69.1%-76.2%)	21.7% (20.7%-23.1%)	59.9% (57.4%-63.1%)
Kentucky	56.3%	66.8% (54.8%-81.2%)	0.84	87.8% (82.1%-93.7%)	55.1% (51.9%-58.6%)	73.9% (70.1%-78.1%)	23% (22.1%-24.1%)	61.4% (58.4%-64.8%)
Louisiana	53.8%	67.2% (55.2%-81.4%)	0.8	87.2% (81.4%-93.4%)	51.1% (47.9%-54.9%)	72% (68.3%-76.3%)	20.5% (19.6%-21.7%)	59.5% (56.5%-62.8%)
Maine	78.3%	36.6% (25.8%-55.3%)	2.14	87.7% (84.7%-92.1%)	55.5% (52.3%-61.2%)	77.2% (75.9%-79.4%)	24.2% (23.3%-25.9%)	64.4% (63.4%-66.2%)
Maryland	75.8%	46.5% (34.3%-65%)	1.63	88.6% (85.2%-93%)	55.1% (51.6%-60.9%)	75.8% (74.4%-77.9%)	23.1% (22%-24.8%)	62.9% (61.8%-64.6%)
Massachusetts	77.7%	51.7% (39.2%-69.7%)	1.5	90.6% (87.5%-94.5%)	57.4% (53.5%-63.3%)	77.9% (76.5%-79.9%)	23.4% (22.3%-25.2%)	64.5% (63.4%-66.1%)
Michigan	56.5%	63.4% (51.1%-78.8%)	0.89	87.5% (81.8%-93.4%)	53.3% (50.2%-57.1%)	72.6% (68.9%-77.1%)	23.2% (22.4%-24.5%)	60.7% (57.7%-64.2%)
Minnesota	64.8%	51.7% (39.2%-69.6%)	1.25	85.4% (80.5%-91.6%)	54.2% (51%-58.8%)	71.9% (69.2%-75.7%)	24.5% (23.7%-25.9%)	60.4% (58.3%-63.5%)
Mississippi	52.8%	68.3% (56.5%-82.2%)	0.77	87.7% (81.8%-93.7%)	50.8% (47.7%-54.5%)	72.4% (68.6%-76.7%)	20% (19.1%-21.2%)	59.6% (56.6%-63.1%)
Missouri	54.2%	51.4% (38.9%-69.3%)	1.06	80.8% (74.3%-89.1%)	46.8% (43.4%-52%)	67.8% (63.6%-73.6%)	19.7% (18.8%-21.3%)	56.2% (52.9%-60.9%)
Montana	56.6%	62.9% (50.5%-78.4%)	0.9	86.6% (80.6%-93%)	55.1% (52%-58.7%)	72.9% (69.1%-77.6%)	24.1% (23.2%-25.2%)	61% (57.9%-64.7%)
Nebraska	55%	59.8% (42.8%-79.1%)	0.92	84.6% (76.2%-92.8%)	51.8% (46.9%-57.8%)	70.3% (64.9%-76.2%)	22.4% (21.1%-24.3%)	58.7% (54.4%-63.4%)
Nevada	62.3%	67.7% (49.2%-86.5%)	0.92	90.1% (82.9%-96.3%)	55.4% (49.2%-62.1%)	75% (70.4%-79.6%)	21.5% (19.7%-23.6%)	61.7% (58%-65.5%)
New Hampshire	82.8%	39.9% (28.7%-58.7%)	2.08	90.5% (88.3%-93.8%)	54.9% (50.9%-61.8%)	80.2% (79.5%-81.4%)	18.1% (16.9%-20.1%)	64.7% (64.1%-65.7%)
New Jersey	75.3%	58.3% (45.7%-	1.29	91.1% (87.8%-95%)	57.6% (53.6%-	76.8% (75.3%-	22.8% (21.6%-	63.4% (62.2%-

		74.9%)			63%)	78.7%)	24.5%)	64.9%)
New Mexico	67.2%	78.5% (68.7%-88.6%)	0.86	94.4% (91.2%-97.3%)	62.4% (60%-64.7%)	78.4% (76.6%-80.1%)	25.9% (25.2%-26.7%)	65.2% (63.8%-66.6%)
New York	75.8%	60.6% (48%-76.7%)	1.25	91.8% (88.7%-95.4%)	57.8% (53.5%-63.5%)	77.4% (76%-79.2%)	21.4% (20.1%-23.2%)	63.4% (62.2%-64.8%)
North Carolina	58.1%	51.7% (37.6%-71.7%)	1.12	83.2% (76.5%-91.2%)	46.2% (41.1%-53.9%)	69.4% (65.1%-75.4%)	17.3% (15.8%-19.6%)	56.7% (53.3%-61.5%)
North Dakota	53.1%	70% (58.4%-83.3%)	0.76	88.4% (82.6%-94.2%)	53.2% (50.6%-56%)	72.6% (68.9%-76.6%)	22.8% (22.1%-23.8%)	60.5% (57.6%-63.7%)
Ohio	56%	50.3% (38%-70.7%)	1.11	81.3% (75.2%-90%)	48.3% (44.9%-54.7%)	68.2% (64.3%-74.5%)	21.3% (20.3%-23.2%)	56.9% (53.8%-62%)
Oklahoma	58.7%	74.6% (63.8%-86.3%)	0.79	91.4% (86.9%-95.8%)	57.8% (55%-60.5%)	76% (73.1%-79%)	22.6% (21.8%-23.5%)	62.7% (60.3%-65.1%)
Oregon	69.6%	42.4% (29.7%-62.9%)	1.64	85.0% (80.4%-91.3%)	52.8% (48.7%-59.9%)	73.1% (70.6%-77.1%)	22.4% (21.3%-24.5%)	60.8% (58.8%-64%)
Pennsylvania	76.1%	54.2% (41.6%-71.7%)	1.4	90.6% (87.4%-94.5%)	56.3% (51.9%-62.5%)	77.3% (75.7%-79.4%)	20.7% (19.4%-22.6%)	63.2% (62%-64.9%)
Rhode Island	75.4%	64.1% (51.8%-79.2%)	1.18	92.6% (89.3%-96.1%)	61.2% (57.8%-65.7%)	78.7% (77.1%-80.6%)	25.2% (24.2%-26.6%)	65.3% (64.1%-66.9%)
South Carolina	56.4%	62.3% (49.9%-78%)	0.91	86.3% (80.3%-92.8%)	51.9% (48.5%-56.2%)	72.2% (68.4%-76.8%)	21% (20%-22.3%)	59.7% (56.7%-63.4%)
South Dakota	63.5%	63.6% (51.3%-78.9%)	1	88.8% (83.9%-94.1%)	55.4% (52.6%-59.1%)	73.3% (70.7%-76.5%)	22.9% (22.1%-24.1%)	60.9% (58.8%-63.4%)
Tennessee	53.8%	65.2% (51.3%-85.3%)	0.82	86.6% (79.9%-94.9%)	51.7% (47.6%-58.2%)	72.3% (67.6%-78.9%)	21.6% (20.4%-23.7%)	60% (56.3%-65.4%)
Texas	62.6%	66.9% (54.9%-81.2%)	0.94	89.4% (84.9%-94.3%)	54.4% (50.9%-58.6%)	73.6% (71%-76.7%)	21.1% (20.1%-22.4%)	60.6% (58.5%-63%)
Utah	50.5%	61.5% (49.1%-77.4%)	0.82	83.7% (77.1%-91.2%)	49% (45.3%-53.3%)	68.8% (64.5%-74%)	19.7% (18.6%-21%)	56.8% (53.4%-61%)
Vermont	61.4%	35.3% (25.8%-52.7%)	1.74	78% (73.2%-85.6%)	50.4% (47.6%-55.8%)	67.8% (64.9%-72.9%)	24.2% (23.5%-25.7%)	57.4% (55.2%-61.4%)
Virginia	64.9%	44.7% (32.7%-63.4%)	1.45	83% (78.1%-89.7%)	50.1% (46.6%-55.7%)	70.7% (67.9%-74.9%)	21.2% (20.3%-22.9%)	58.7% (56.6%-62.1%)
Washington	69.2%	41.7% (30.1%-60.5%)	1.66	84.5% (80.2%-90.5%)	50.9% (47.3%-57%)	72.3% (70.1%-75.7%)	21.6% (20.6%-23.3%)	60% (58.3%-62.8%)
West Virginia	32%	61.3% (48.8%-	0.52	76.9% (67.6%-87.6%)	41.6% (37.6%-	65.4% (58.3%-	14.4% (13.2%-	53% (47.3%-60%)

		77.2%)			46.2%)	74.2%)	15.8%)	
Wisconsin	63.4%	51.4% (39.6%-71%)	1.23	84.7% (79.7%-91.7%)	52.9% (49.7%-58.6%)	71.7% (68.8%-76.4%)	23.5% (22.7%-25.3%)	60.1% (57.8%-63.8%)
Wyoming	51.7%	72.3% (55.3%-91.4%)	0.71	89.1% (80.5%-97.1%)	56.2% (50.7%-62.6%)	74.7% (68.5%-81.3%)	23.7% (22.1%-25.8%)	62.1% (57.2%-67.5%)

*Received at least one COVID-19 vaccine dose

** Assuming the base-case waning functions.

*** Assuming the base-case waning functions and the medium immune evasion scenario.

FIGURE LEGENDS

Figure 1: Estimated percentage *immunologically exposed* on December 1, 2021, for each US county and state.

Footnote: The background coloring indicates the state-specific distribution of immunity as a function of infections and vaccinations. Black dots represent counties in a state, red dots the state average. The orange diamond represents the state-population-weighted national averages of the percentage ever infected and vaccinated (this does not represent the national average of immunity because the calculation for immunity is state-specific).

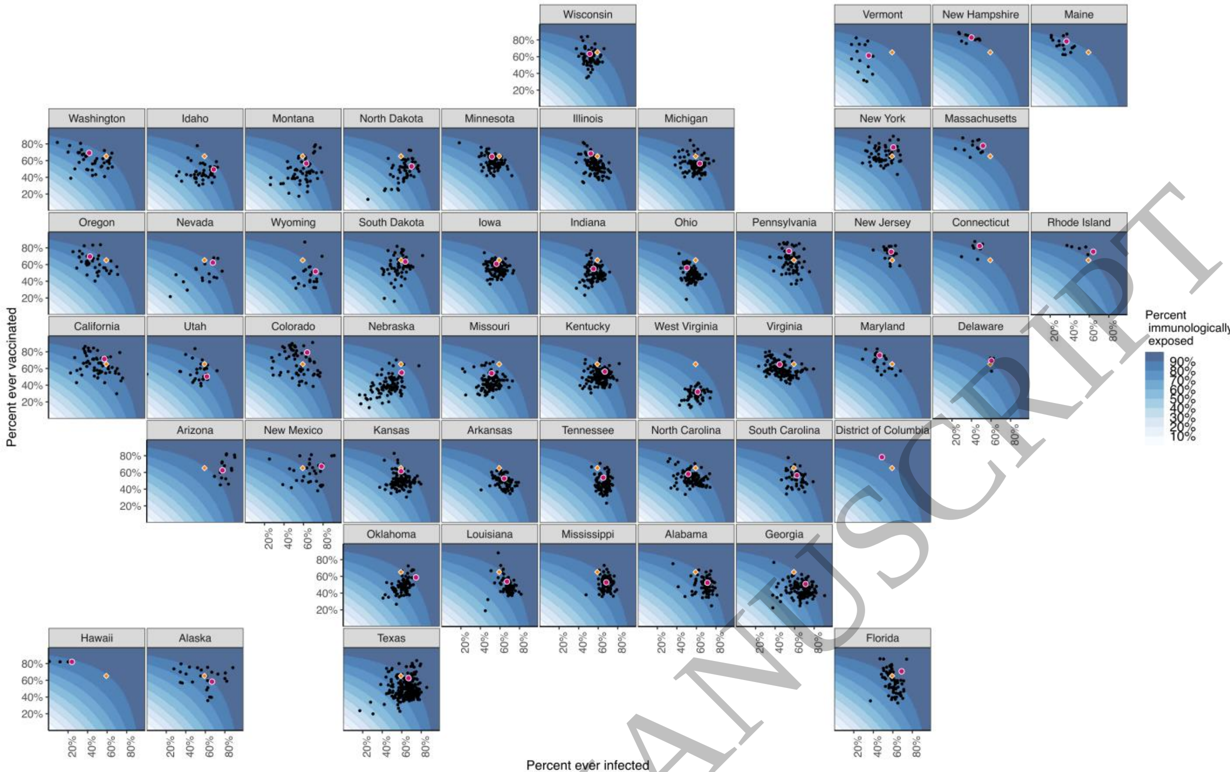
Figure 2: State-level estimates and uncertainty intervals of the percentage *immunologically exposed*, *effectively protected* against infection, and *effectively protected* against severe disease over time, with estimates of *effective protection* against Omicron infection under three immune escape scenarios.

Figure 3: County-level estimates of the percentage of the population *effectively protected* against infection at four time-points between January 31, 2021 and December 1, 2021. Counties excluded due to missing or insufficient data are colored yellow.

Figure 4: Relative contribution of prior infection and vaccination to population immunity for each county at four time-points between January 31, 2021 and December 1, 2021.

Footnote: The percentage ever infected and the percentage vaccinated are categorized with cut-off scores of 40%, 50% and 60%. These values which roughly corresponds to the quantile breakpoints of the estimates of ever infected and vaccinated on December 1, 2021.

1

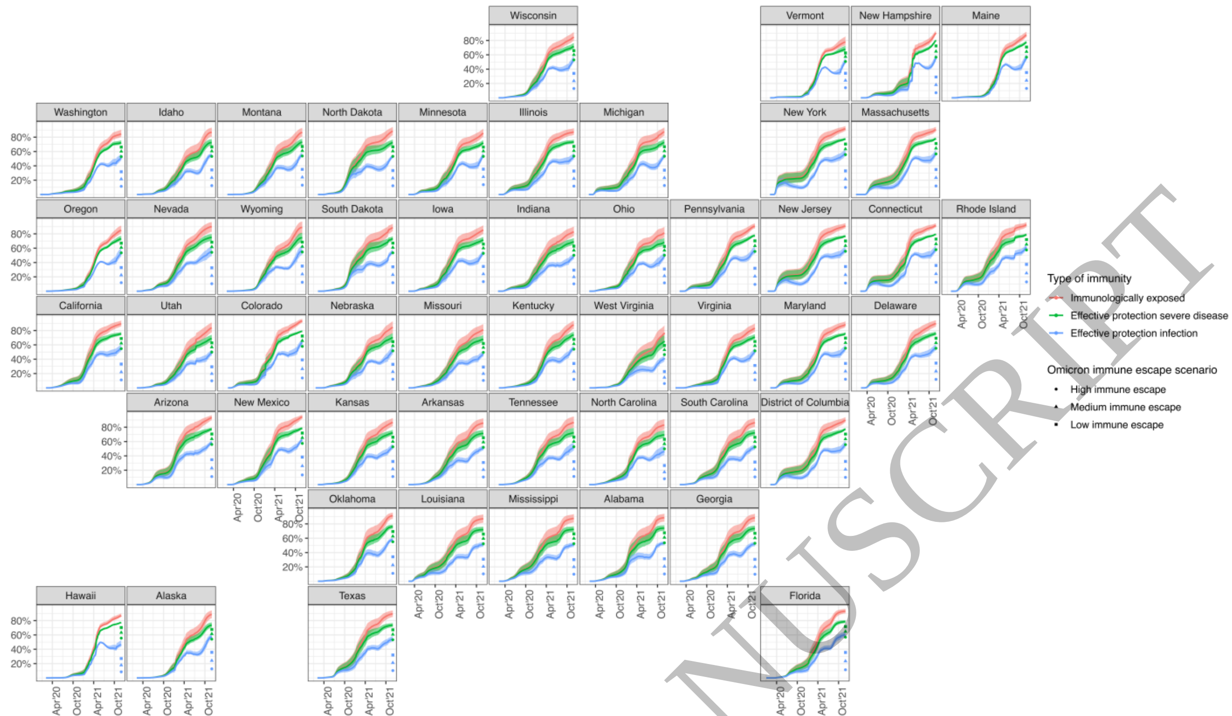


2 **Figure 1**

3 **165x103 mm (.89 x DPI)**

4

1



2 **Figure 2**

3 **165x97 mm (.89 x DPI)**

4

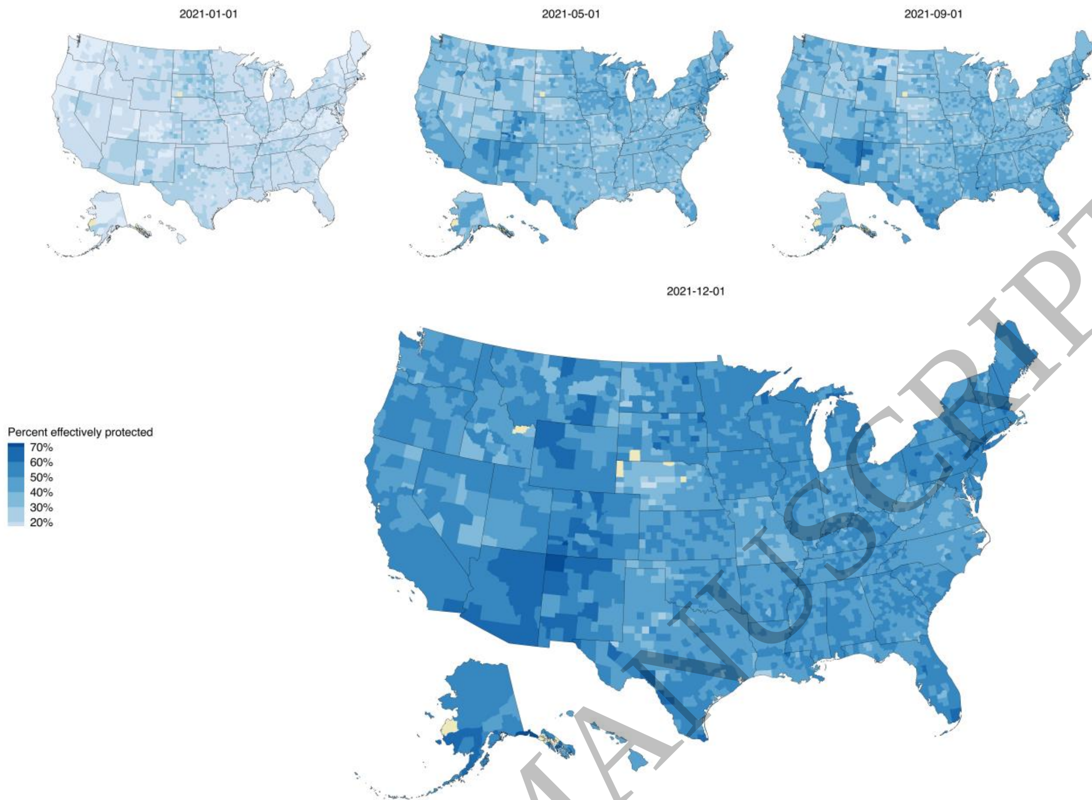


Figure 3
165x97 mm (.89 x DPI)

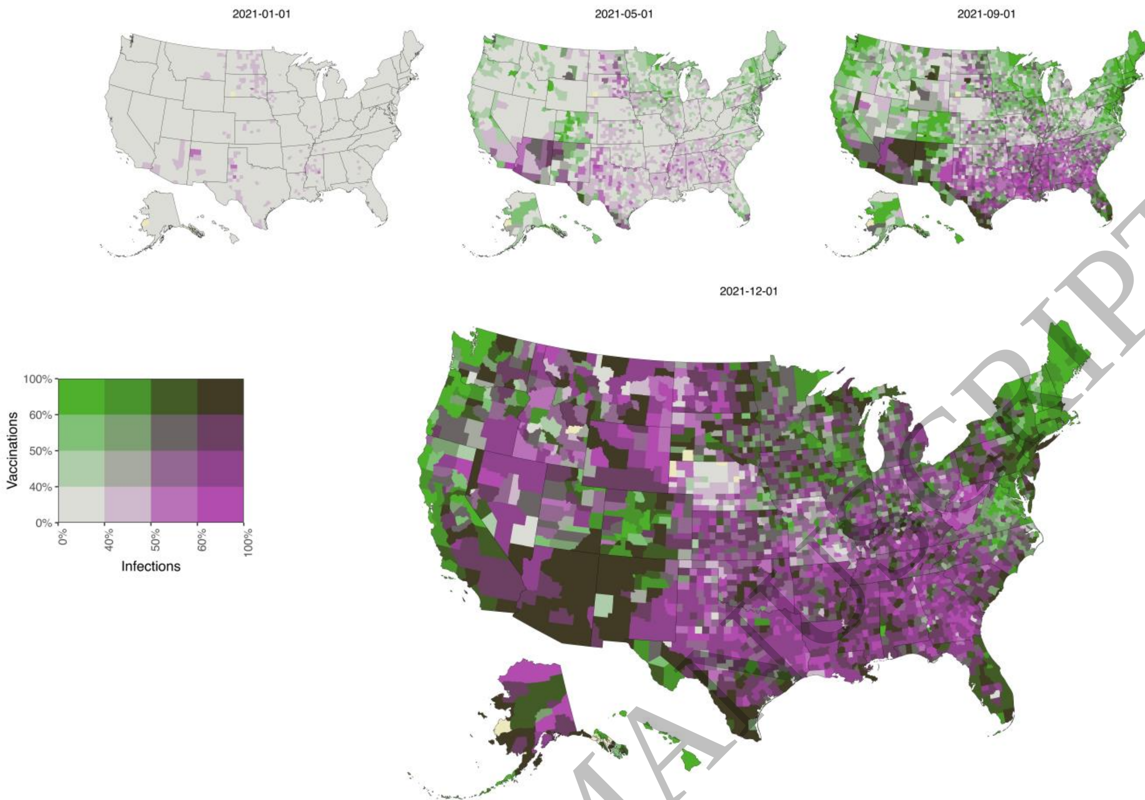


Figure 4
165x97 mm (.89 x DPI)