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SARS-CoV-2 Attack Rate and Population Immunity in Southern New England, March 2020 to May 2021

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Abstract

IMPORTANCE In emergency epidemic and pandemic settings, public health agencies need to be able to measure the population-level attack rate, defined as the total percentage of the population infected thus far. During vaccination campaigns in such settings, public health agencies need to be able to assess how much the vaccination campaign is contributing to population immunity; specifically, the proportion of vaccines being administered to individuals who are already seropositive must be estimated.

OBJECTIVE To estimate population-level immunity to SARS-CoV-2 through May 31, 2021, in Rhode Island, Massachusetts, and Connecticut.

DESIGN, SETTING, AND PARTICIPANTS This observational case series assessed cases, hospitalizations, intensive care unit occupancy, ventilator occupancy, and deaths from March 1, 2020, to May 31, 2021, in Rhode Island, Massachusetts, and Connecticut. Data were analyzed from July 2021 to November 2021.

EXPOSURES COVID-19–positive test result reported to state department of health.

MAIN OUTCOMES AND MEASURES The main outcomes were statistical estimates, from a bayesian inference framework, of the percentage of individuals as of May 31, 2021, who were (1) previously infected and vaccinated, (2) previously uninfected and vaccinated, and (3) previously infected but not vaccinated.

RESULTS At the state level, there were a total of 1 160 435 confirmed COVID-19 cases in Rhode Island, Massachusetts, and Connecticut. The median age among individuals with confirmed COVID-19 was 38 years. In autumn 2020, SARS-CoV-2 population immunity (equal to the attack rate at that point) in these states was less than 15%, setting the stage for a large epidemic wave during winter 2020 to 2021. Population immunity estimates for May 31, 2021, were 73.4% (95% credible interval [CrI], 72.9%-74.1%) for Rhode Island, 64.1% (95% CrI, 64.0%-64.4%) for Connecticut, and 66.3% (95% CrI, 65.9%-66.9%) for Massachusetts, indicating that more than 33% of residents in these states were fully susceptible to infection when the Delta variant began spreading in July 2021. Despite high vaccine coverage in these states, population immunity in summer 2021 was lower than planned owing to an estimated 34.1% (95% CrI, 32.9%-35.2%) of vaccines in Rhode Island, 24.6% (95% CrI, 24.3%-25.1%) of vaccines in Connecticut, and 27.6% (95% CrI, 26.8%-28.6%) of vaccines in Massachusetts being distributed to individuals who were already seropositive.

CONCLUSIONS AND RELEVANCE These findings suggest that future emergency-setting vaccination planning may have to prioritize high vaccine coverage over optimized vaccine

(continued)

Key Points

Question What proportion of individuals living in southern New England had immunity to SARS-CoV-2, either through past infection or vaccination, by May 31, 2021?

Findings This case series analysis for Rhode Island, Massachusetts, and Connecticut revealed that two-thirds of residents were immune to SARS-CoV-2 by May 31, 2021. The population immune fraction was lower than desired because 27% of vaccines during the winter to spring 2021 vaccination campaign were administered to individuals who were already seropositive.

Meaning These findings suggest that SARS-CoV-2 population immunity was overestimated in summer 2021 and that future emergency-setting vaccination campaigns may need to exceed traditional coverage goals.

+ Supplemental content

Author affiliations and article information are listed at the end of this article.

Abstract (continued)

distribution to ensure that sufficient levels of population immunity are reached during the course of an ongoing epidemic or pandemic.

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Introduction

Public health response and management of the COVID-19 pandemic met significant challenges at every stage of the pandemic in 2020 and 2021. Clinical experience and trial data accrued during the first and most deadly[1,2] wave of March to April 2020, leading to improvements in care for hospitalized patients.[3-6] Understanding of mobility, lockdown, and contact tracing policies improved by the summer of 2020, allowing for preparation of school reopening plans for autumn of 2020.[7-9] However, in autumn of 2020, substantial variation in estimates reported from several large seroprevalence studies[10-12] meant that we knew little at the time about the true number of individuals who had been infected between March 2020 and November 2020 or how population susceptibility would drive the winter epidemic wave of 2020 to 2021.

Real-time estimation of seroprevalence or attack rate is challenging. Model-based estimates of attack rate using daily reported case numbers require us to be able to estimate the number of unreported or untested symptomatic cases and the number of asymptomatic infections. In this estimation procedure, an assumed infection fatality rate (IFR),[13,14] hospitalization incidence,[1,15] or death incidence[16] can be used to work backward to infer the numbers of unreported cases or unreported infections. Alternatively, surveys of health care–seeking behavior can be used.[17,18] This means that age structure is necessary in these reporting streams, as the rate of asymptomatic SARS-CoV-2 infection, hospitalization probability, and death probability all vary substantially by age.[19-21] When hospitalization incidence is not available (eg, owing to underreporting[1]), data streams for death, current hospitalization, current numbers of patients in intensive care units (ICUs) and using ventilators can be used to estimate the incidence of hospitalization.

Estimating attack rate with cross-sectional serological data presents its own unique requirements, including preplanned periodic serum collections[22-24] and a high-throughput validated assay; results will still be reported with a 1-month lag owing to the delay from infection to immunoglobin G positivity in a serological assay. Since the beginning of the COVID-19 pandemic in the US, the Centers for Disease Control and Prevention (CDC), with a large group of commercial and nonprofit partners,[25-27] has been collecting cross-sectional serum samples from blood donors and residual samples from routine laboratory testing. These sample collections are a valuable epidemiological resource, but for most states, seroprevalence estimates are not translatable into attack rate estimates because the seroprevalence estimates move up and down through time while the attack rate can only go up.[28] These nonmonotonic measurements are common in serology: if an antibody assay threshold is set too high, the assay shows recent seroprevalence rather than cumulative seroprevalence, resulting in systematic underestimation of the number of individuals who have been infected. A simple example can be seen for Massachusetts infection seroprevalence, measured as 10.2% in late April 2021,[26] at which point 9.1% of the state's residents had reported confirmed positive results for SARS-CoV-2 infection. This would mean that the ratio of infections to confirmed cases was 1.1 to 1 in Massachusetts, which is inconsistent with our knowledge of SARS-CoV-2 infection, clinical progression, and reporting. This ratio is typically estimated between 2.0 to 1 and 6.0 to 1, depending on methods and the period being analyzed.[13,14,27] In this analysis, we present a model-based reconstruction of the SARS-CoV-2 attack rate and population immunity curves for 3 New England states: Massachusetts, Connecticut, and Rhode Island, for the first 15 months of the pandemic.

Methods

This case series used publicly available population-level count data; all data points were fully deidentified. Studies on publicly available data are exempt from human participants review and informed consent under 45 CFR 46.104 (d)(4)(i).[29] We used the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline for clinical observational studies.

A published bayesian inferential framework based on a dynamical epidemic model (eFigure 1 in the Supplement) was used to fit case, hospitalization, and death data from Massachusetts, Connecticut, and Rhode Island.[1,30] We collected 11 daily data streams from each state: (1) cumulative confirmed cases, (2) cumulative confirmed cases by age, (3) cumulative hospitalized cases, (4) cumulative hospitalized cases by age, (5) number of patients currently hospitalized, (6) number of patients currently in an ICU, (7) number of patients currently receiving mechanical ventilation, (8) cumulative deaths, (9) cumulative deaths by age, (10) cumulative hospital deaths, and (11) cumulative hospital discharges. The age and totals data streams are separated because the age-structured data do not always sum to the correct totals, have more missingness, and require a different statistical approach in the model fitting (eAppendix 1 in the Supplement). Daily time points from March 1, 2020, to June 6, 2021, were included in this analysis. Details on Connecticut data sources are in eAppendix 2 in the Supplement; Rhode Island and Massachusetts data sources are described elsewhere.[1]

Statistical Analysis

Weekly age-structured SARS-CoV-2 vaccination numbers were obtained separately for the 3 states,[31-34] and vaccinated individuals receiving their final vaccine dose were moved from the susceptible compartment in the dynamical model to the recovered compartment whenever a individual who was seronegative was vaccinated. All modeling and data fitting were performed with a daily time step, and weekly vaccination data were configured into a daily time series through simple linear interpolation. The model allows for vaccination of individuals who are seropositive. In the model, the fraction

$$a_{t,neg} = \frac{S_t}{S_t + E_t + A_t + (1 - [1 - p_{EA}]\rho_t)(1 - p_v)R_t}$$

represents the total fraction of nonsymptomatic, nonhospitalized individuals who are antibody-negative and virus-negative at time t. The denominator is the candidate pool of individuals for whom a COVID-19 vaccine would be immediately recommended. The uppercase letters represent the numbers of individuals in each model compartment at time t for individuals who were susceptible (S), exposed individuals (E), individuals who were asymptomatically infected with SARS-CoV-2 (A), and individuals who recovered from a SARS-CoV-2 infection that did not require hospitalization or those who have been vaccinated (R). The fraction p_{EA} represents the fraction of individuals who were infected but who never developed symptoms (different for every age group), and the reporting rate ρ_t represents the fraction of symptomatic individuals who were tested, confirmed positive, and were thus aware that they had already had COVID-19. The fraction p_v is the total fraction of the population (by age group) that has been vaccinated thus far. Thus, the denominator's modified R-term seeks to approximate the nonvaccinated fraction of the recovered group who were unaware that they have recovered from a SARS-CoV-2 infection, and thus would have sought vaccination between January and May 2021 at the same rate as individuals who had never been infected (only a fraction of these were vaccinated in the model, depending on each state's data for that week). The model reports the total number of vaccines given to individuals in the susceptible class S and the total number of vaccines given to individuals in all classes.

The model accommodates temporally varying patterns of clinical care and changing age-contact rates. To model either a change in clinical management or an increase or decrease in the vulnerability

of the current patient pool (ie, the risk of progression to hospitalization or death), we allow the transition probability from medical floor stay to ICU to vary throughout the epidemic.

We report 2 types of IFRs. The population-weighted IFR is the probability of death, if infected, for a person sampled at random from a population with a particular age structure. The epidemic IFR is infections weighted; it is the probability of death for a randomly sampled individual who is infected during a particular epidemic phase. All estimates are presented as medians and 95% credible intervals (CrI) from 1000 posterior samples. Prior distributions are shown in eTable 1 in the Supplement.

Analyses were conducted using the R programming language version 4.1.3 (R Project for Statistical Computing) and the Python programming language version 3.8.12 (Python Software Foundation). Data were analyzed between July 2021 and November 2021.

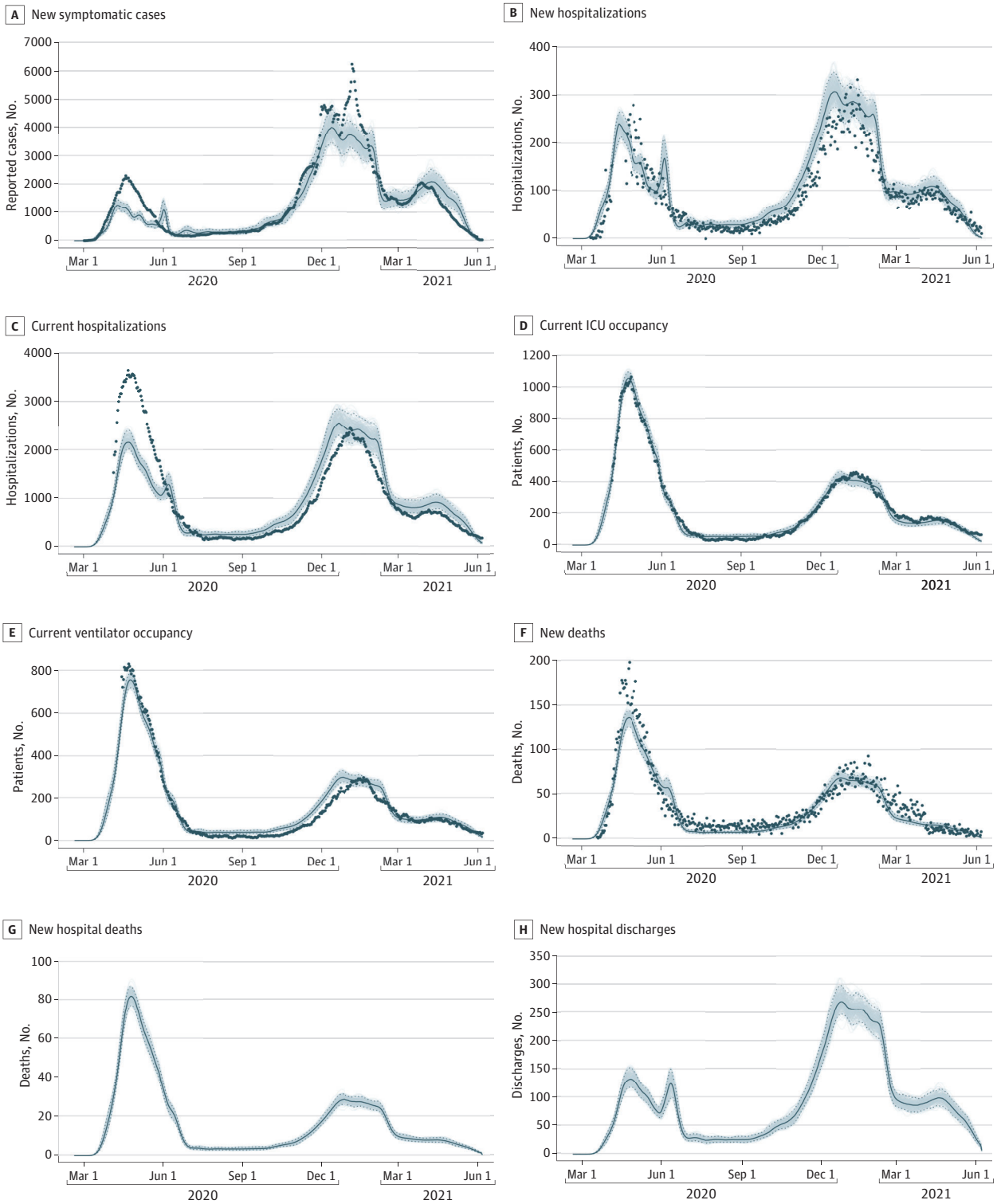
Results

A total of 1 160 435 polymerase chain reaction testing–confirmed COVID-19 cases were reported in Massachusetts, Connecticut, and Rhode Island between March 1, 2020, and June 6, 2021. The median age among individuals with confirmed COVID-19 was 38 years, with 19.7% of individuals with COVID-19 older than 60 years and 17.9% of individuals with COVID-19 younger than 20 (eTable 2 in the Supplement). A total of 85 221 individuals with COVID-19 (7.3%) were hospitalized and 28 554 individuals (2.5%) died. In the 3 included states, 6 196 902 individuals, 53.8% of the population, were vaccinated by June 6, 2021.

State-level inference shows model fits that accurately describe the dynamics of ICU occupancy, ventilator occupancy, and daily death counts in all 3 states during the study period. Rhode Island's inferred epidemic curve in particular shows close fits to all 8 non–age structured data streams (eFigure 2 in the Supplement), likely owing to the completeness of hospital reporting available in a small state. Case and hospitalization data fit well in all states, with the exception of the case incidence data and current hospitalization data in Massachusetts, which the model underfit for the March to April 2020 epidemic wave (**Figure 1**). In addition, high variance in new case incidence in Connecticut for the March to April 2020 wave and the major winter wave of 2020 to 2021 suggest that the model may not be capturing complete heterogeneity in transmission dynamics and case reporting (eFigure 3 in the Supplement). Both the data and the model, across all data streams for all 3 states, clearly reconstruct the early epidemic wave of March to April 2020, the summer lull of 2020, the major winter wave of 2020 to 2021, and the lagging wave of the Alpha (B.1.1.7) variant in March to April 2021. All parameter posterior distributions are shown in eFigures 4 through 10 in the Supplement.

Using our model's inferred reporting rate (**Figure 2**A) and an external estimate[21] of the asymptomatic fraction of each age group's infections, we inferred that as of May 31, 2021, the population-level attack rates were 41.5% (95% CrI, 40.4%-42.7%) in Rhode Island, 25.8% (95% CrI, 25.5%-26.3%) in Connecticut, and 28.0% (95% CrI, 27.1%-29.0%) in Massachusetts. Since summer 2020, attack-rate estimations were robust to the differing amounts of data included in the analyses (**Figure 3**). Attack rate estimates in Connecticut were consistent with those reported in a study by Morozova et al,[35] and attack rate comparisons in Rhode Island and Massachusetts were consistent with other model-based estimates[13,14] as described in our previous study.[1] Comparison with CDC seroprevalence data were more challenging, since there was a discrepancy between the 2 types of estimates presented (eAppendix 3 in the Supplement). By January 31, 2021, approximately 2.1% to 2.3% of each state's population was vaccinated, with this vaccinated fraction reaching 8.0% to 9.6% by February 28, 2021. Using the modeled number of infections, daily data on vaccinations that were integrated into the model, and the modeled number of individuals who were already seropositive who would have received vaccination, we inferred population immunity levels of 73.4% (95% CrI, 72.9%-74.1%) in Rhode Island, 64.1% (95% CrI, 64.0%-64.4%) in Connecticut, and 66.3% (95% CrI, 65.9%-66.9%) in Massachusetts for May 31, 2021 (**Figure 4**; eTable 3 and eTable 4 in the

Figure 1. Massachusetts Fit of Model to Data



Hospital discharge data and death data separated by in and out of hospital were not available in Massachusetts. Dots indicate absolute daily counts; line, model median from the posterior; and shading, 95% credible region. Similar fits to 11 Rhode Island data streams are shown in eFigure 2 in the Supplement and 7 Connecticut data streams are in eFigure 3 in the Supplement.

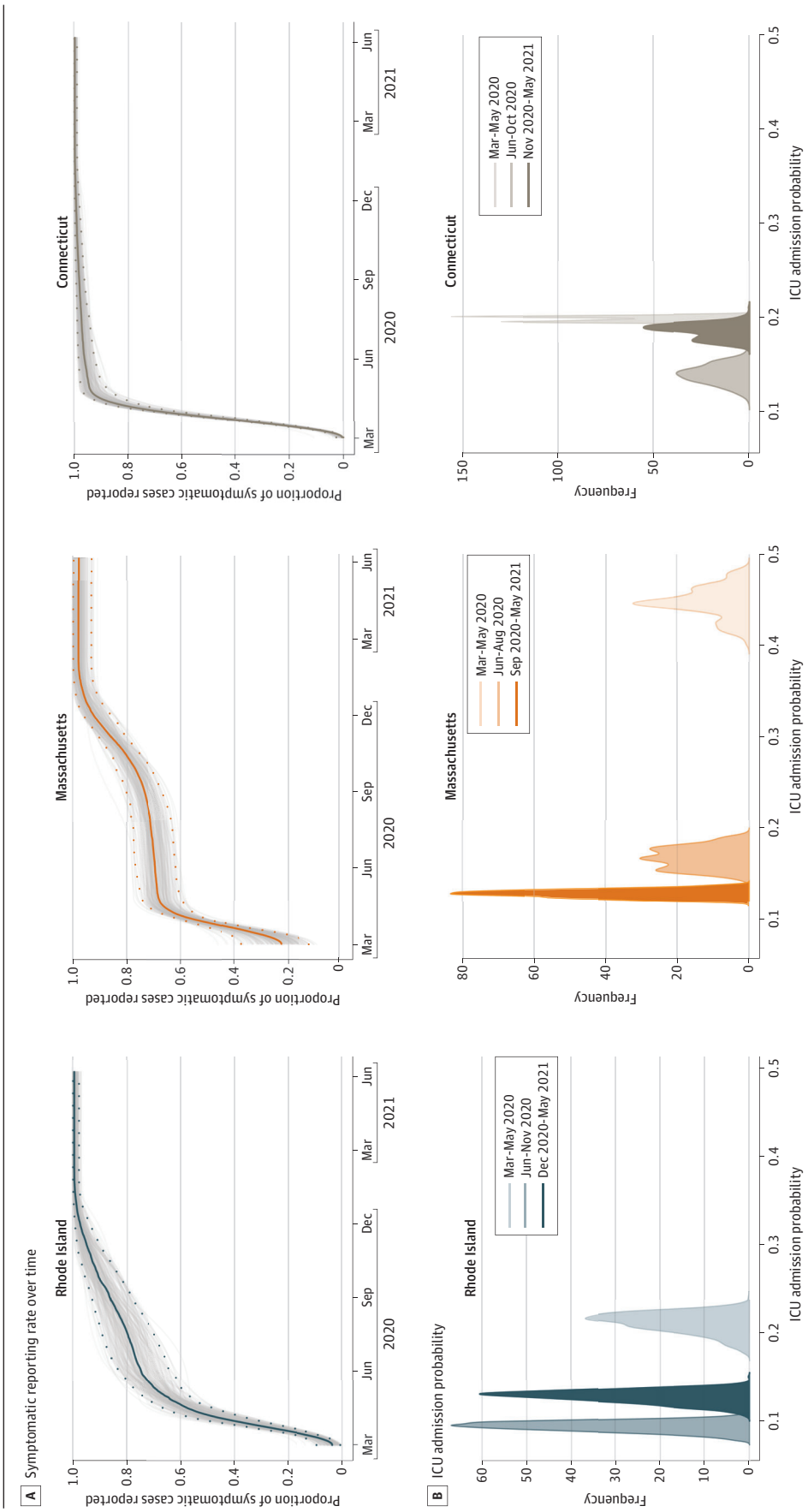
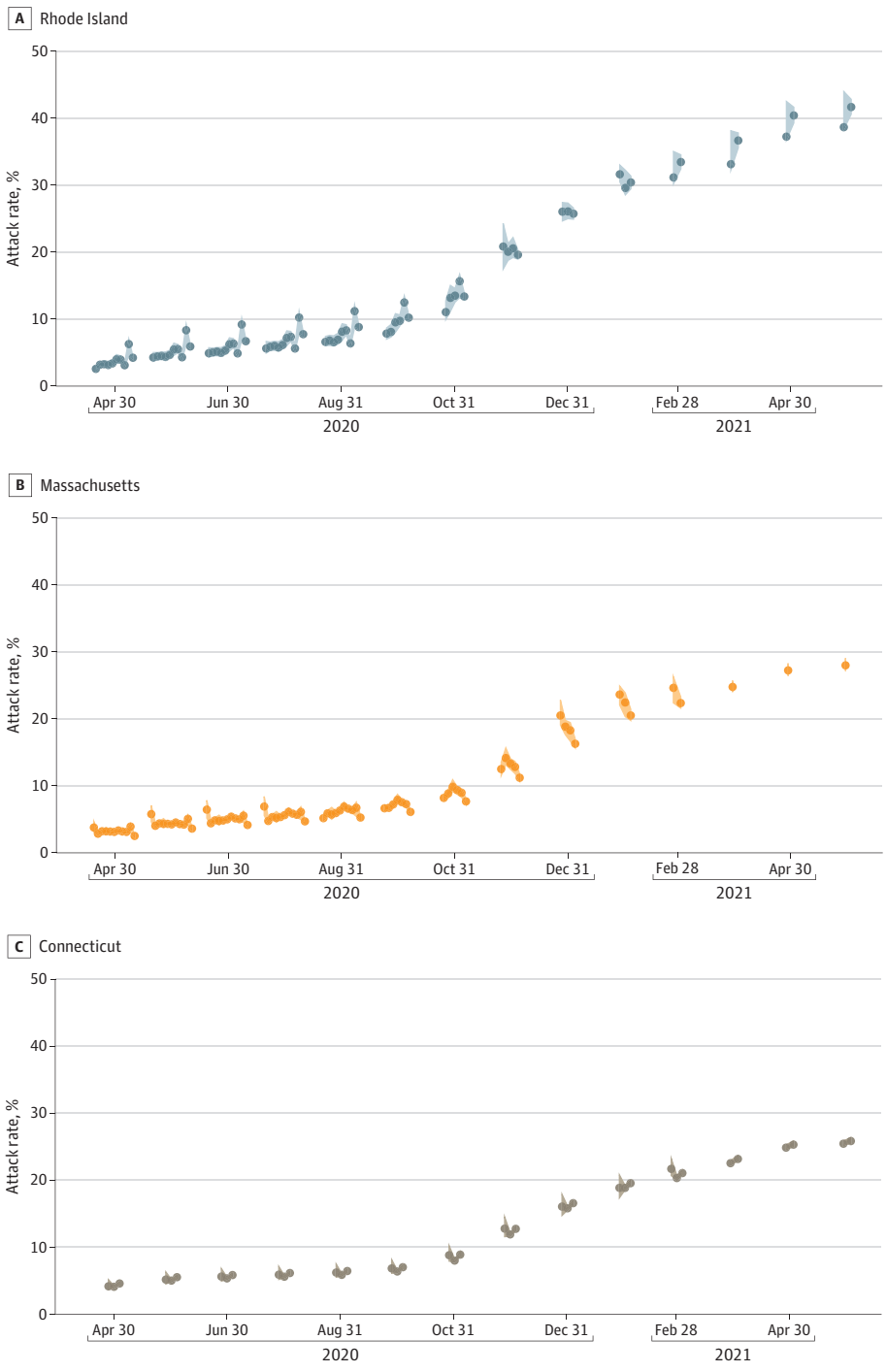


Figure 2. Posterior Distributions for Reporting Rate and Intensive Care Unit (ICU) Admission Probability

Posterior distributions for A, the per-symptomatic-case reporting rate, ie, the fraction of symptomatic COVID-19 cases that were reported to the respective Department of Health reporting system, fit with an I-spline to allow an increasing level of testing and reporting through time; and B, ICU admission probability, per hospitalized case, for different phases of the epidemic.

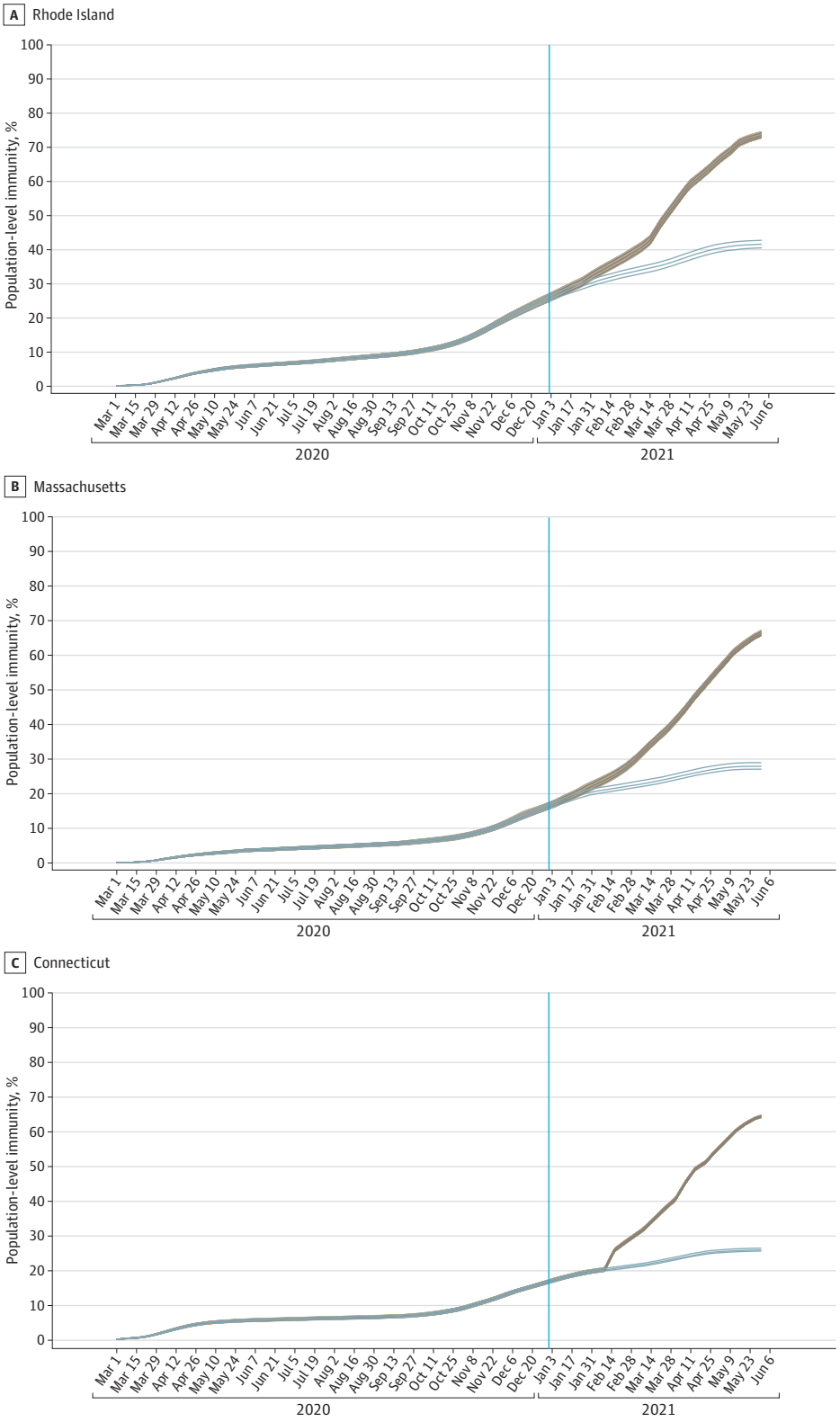
Supplement). This implies that more than 33% of southern New England was immunologically naive when the Delta variant reignited a wave of infections in late July 2021. From the model, we infer that the percentage of vaccines administered to individuals who were seropositive was 34.1% (95% CrI, 32.9%-35.2%) in Rhode Island, 24.6% (95% CrI, 24.3%-25.1%) in Connecticut, and 27.6% (95% CrI, 26.8%-28.6%) in Massachusetts. The **Table** provides a breakdown of infection and vaccination status in all 3 states; these estimates are consistent with those of a study by Moghadas et al[36] that

Figure 3. Robustness of Attack Rate Estimation



Each dot indicates 1 attack rate estimated with data available only through a particular date. For example, for April 30, 2020, 10 estimates are available for Rhode Island, 11 estimates are available for Massachusetts, and 3 estimates are available for Connecticut; all of these estimates were obtained at different times with different amounts of data available. The dots are ordered from left to right chronologically, with the right-most estimates using the most data (and being done the latest). Shaded areas indicate 95% credible intervals for each estimate.

Figure 4. Population Immunity



Blue lines indicate total percentage of each state's population that has been infected; brown lines, percentage of the population that has either been infected or vaccinated (counting only once individuals who have been both infected and vaccinated); vertical line, January 1, 2021. The 3 lines shown are medians and boundaries of 95% credible intervals. Exact estimates are shown in eTables 3 and 4 in the Supplement. Note that the population-level immunity estimate (y-axis) shows the percentage of individuals that have some level of immunity to the Alpha and pre-Alpha variants of SARS-CoV-2.

used a direct IFR-based deaths-to-infections translation to estimate that approximately half of all individuals who had been previously infected received vaccination.

The mortality impact of the SARS-CoV-2 epidemic in these 3 states was severe. In Connecticut, 0.229% of residents died during the first 15 months of the epidemic; 0.248% of Rhode Island residents and 0.249% of Massachusetts residents died during this same time period, indicating that the epidemic was approximately 8% to 9% more deadly in Rhode Island and Massachusetts than in Connecticut. Using the inferred attack rates over the first 15 months of the epidemic, we estimate the 15-month epidemic IFR in the 3 states as 0.62% (95% CrI, 0.60%-0.64%) in Rhode Island, 0.89% (95% CrI, 0.87%-0.90%) in Connecticut, and 0.89% (95% CrI, 0.86%-0.92%) in Massachusetts. Rhode Island had an estimated 55% to 60% more infections per population than Connecticut or Massachusetts, and this cannot be explained by any age-specific differences in transmission, indicating that Rhode Island had a larger and broader epidemic across all age groups. The lower epidemic IFR in Rhode Island suggests that the larger epidemic extended to less vulnerable groups (ie, groups less likely to progress to hospitalization and death), lowering the mean fatality rate for the epidemic as a whole.

As in previous analyses showing differing patterns of clinical progression during different epidemic phases,[1,30] we included changepoints in the ICU admission fraction in our model to allow for changes in clinical treatment for hospitalized patients. In Rhode Island and Massachusetts, the ICU admission fraction dropped substantially from the March to April 2020 epidemic wave to the summer to fall transmission period in 2020; Connecticut estimates were less reliable because ICU data only began to be reported in July 2020. In early summer 2020, the age-adjusted probability of ICU admission decreased from 0.21 (95% CrI, 0.18-0.23) to 0.09 (95% CrI, 0.08-0.10) in Rhode Island, 0.45 (95% CrI, 0.42-0.48) to 0.17 (95% CrI, 0.15-0.19) in Massachusetts, and 0.20 (95% CrI, 0.19-0.20) to 0.14 (95% CrI, 0.12-0.16) in Connecticut (Figure 2B). The estimated population-weighted IFR estimate for the March to May 2020 phase of the epidemic was 1.64% (95% CrI, 1.52%-1.72%) for Rhode Island, 1.55% (95% CrI, 1.45%-1.62%) for Connecticut, and 2.40% (95% CrI, 2.22%-2.51%) for Massachusetts, approximately 2- to 3-fold higher than during later phases of the pandemic, consistent with previous estimates.[1,2]

Discussion

This case series found that approximately 27% of vaccines in Connecticut, Massachusetts, and Rhode Island were administered to individuals with previous infection, which likely biased the confidence of policy makers and epidemiologists in the vaccination rollout's ability to generate population immunity and prevent future waves of infection. In general, during the course of the COVID-19 pandemic, an inability to plan several months ahead was partially caused by an inability to quickly and correctly assess the amounts of infection and immunity in the population at a given moment.[37] The epidemiology community did not foresee the beginning of the Delta wave in July 2021[38] because there were no accurate state-level estimates of population susceptibility. This had important implications, since approximately 140 000 individuals died in the US during the Delta variant period that lasted from July to October. In addition, we did not have an approach for coanalyzing the waning epidemic dynamics of January to May 2021 with the vaccine rollout that was occurring

Table. Previous Infection Status and Vaccination Status of Included Populations as of May 31, 2021

State	Residents, % (95% credible interval)			
	Previously infected and vaccinated	Vaccinated but not previously infected	Previously infected but not vaccinated	Immunologically naive[a]
Rhode Island	16.5 (16.0-17.1)	31.9 (31.4-32.5)	25.0 (24.4-25.6)	26.6 (25.9-27.1)
Massachusetts	14.7 (14.2-15.2)	38.4 (37.9-38.8)	13.3 (12.8-13.9)	33.7 (33.1-34.1)
Connecticut	12.5 (12.4-12.8)	38.4 (38.1-38.5)	13.2 (13.1-13.5)	35.9 (35.6-36.0)

[a] No history of infection or vaccination.

simultaneously. As a matter of policy for the next emergency-initiated vaccination campaign, it will be necessary to consider excess vaccination as an option to ensure that we are not attempting a so-called soft landing[39,40] with just enough vaccine distribution to reach an uncertain threshold of population immunity and a slow decline of case rates.

The 3 state epidemic profiles differed. Rhode Island's epidemic was larger but less severe on a per-infection basis. One potential explanation for Rhode Island's epidemic profile is a positive correlation between susceptibility and vulnerability. During an epidemic in a heterogeneously exposed population, the most susceptible individuals are infected first.[41,42] This would mean that in the larger Rhode Island epidemic, the average susceptibility and the average vulnerability would be lower than those in Massachusetts or Connecticut, resulting in fewer hospitalizations per infection and a lower IFR. For Massachusetts, cumulative hospitalization counts are self-reported by hospitals and have not been validated for completeness (Massachusetts Department of Public Health, email and telephone communications, August to October 2020). If hospitalization incidence is undercounted in Massachusetts by 30%, then Massachusetts and Connecticut would have nearly identical epidemic profiles, with 9.4% of the population symptomatically infected, 0.87% of the population hospitalized, and a hospital fatality rate in Massachusetts that is approximately 10% higher than in Connecticut. This could be one of the reasons for the discrepancy between the hospital incidence and current hospitalization data stream in Massachusetts.

The most important information to integrate into the next phase of attack rate estimation and population immunity estimation in the US is the waning rate of SARS-CoV-2 antibodies. Waning antibody rates are now known for the short-term postinfection[43-46] and postvaccination periods,[47-51] suggesting that antibody waning cannot be ignored for SARS-CoV-2 seroprevalence analyses stretching longer than 1 year. Estimates of waning antibodies will allow for the estimation of recent attack rates,[52] which can either be reported as such or chained together to provide an annual attack rate estimate. Although the initial live integration of these data streams will no doubt be challenging, the benefit will be a situationally aware susceptibility estimate that will allow us to evaluate the invasion ability of a new high-transmissibility variant or immune-escape variant. For Omicron specifically, the reinfection hazards presented by Pulliam et al[53] indicate that the infected but not vaccinated portion of the population can be viewed as approximately 2-fold as likely to be infected as they were in the previous Delta and Alpha waves. The potential cost of not providing these live attack rate and susceptibility estimates is a repeat of summer 2021, when epidemiologists were caught unaware of the immediate risk posed by the introduction of the Delta variant in a still highly susceptible population.

Limitations

This study has some limitations. The major limitation in our assessment of the overlap between past infections and vaccination is a lack of data on how individual choices were made to vaccinate or not. Vaccination was not discouraged for individuals with past infection, and most public health communication at the time informed individuals with COVID-19 that they were vaccine-eligible as soon as symptoms resolved. This means that our assumption that individuals with past confirmed SARS-CoV-2 infections would have delayed their vaccinations likely resulted in an underestimate of the vaccine supply that was distributed to individuals with some level of immunity. Additionally, vaccine mandates put in place for high-exposure groups (eg, health care workers, other essential workers, employees working in indoor venues) imply that past exposure and current vaccination should correlate positively. On the other hand, provaccine stances are positively correlated with other types of public health adherence, such as masking or distancing behaviors. This contributes a negative correlative effect between past infection and vaccination. Data to assess the magnitudes of these 3 behavioral associations are not currently available from state departments of health.

Conclusions

This case series found that ostensibly highly vaccinated populations were susceptible to a surge of Delta infections in July 2021 because we overestimated the spring 2021 vaccination campaign's effect on population immunity. The real-time exercise organized for the purpose of providing these monthly attack-rate estimates[54] shows the value of understanding an epidemic's susceptibility curve while it is changing. Live attack rate estimation can be sharpened by the addition of a data stream that connects case numbers to a whole-population measure. The most direct approach to this is to perform weekly PCR-testing on random samples of the population (or a cohort) to obtain basic live prevalence curves during an epidemic.[55] Tools like this are resource-intensive but potentially worth the cost; the ability to directly integrate them into sample processing pipelines and data analysis pipelines will hopefully motivate us to include live attack rate and susceptibility estimation into preparation for our next major uncontrolled epidemic or pandemic.

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Administrative, technical, or material support: Leighow, Gentilesco, Pritchard, Crawford, Boni.

Supervision: Pritchard, Hanage, Hanks, Boni.

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SUPPLEMENT.

Supplemental Online Content

Tran TNA, Wikle NB, Yang F, et al. SARS-CoV-2 attack rate and population immunity in southern New England, March 2020 to May 2021. *JAMA Netw Open*. 2022;5(5):e2214171. doi:10.1001/jamanetworkopen.2022.14171

This supplemental material has been provided by the authors to give readers additional information about their work.

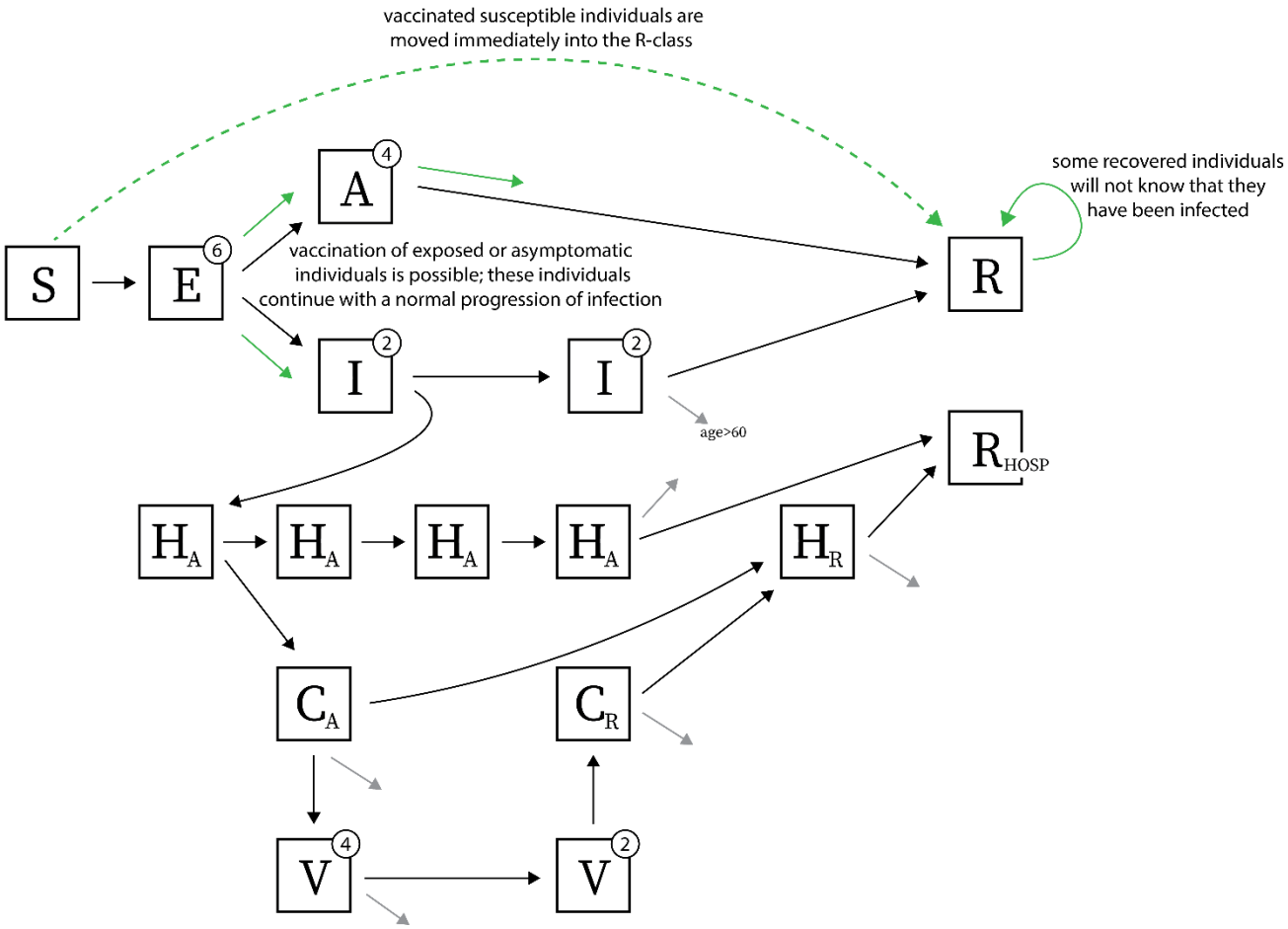
eAppendix 1. Model Description

Full model description and equations are in Section 2 of the Supplementary Materials to Wikle et al[1]. In summary, we use a 30-compartment epidemiological model based on a traditional SEIR framework but with detailed class structure added for the advanced clinical stages of SARS-CoV-2 infection. The model includes twelve types of classes for individuals who are susceptible and immunologically naïve (S), exposed (E), asymptomatic (A), infected and symptomatic (I), acute-phase hospitalized but not in the ICU (H_A), in acute-phase critical care but not yet on a ventilator (C_A), on a ventilator (V), in critical care after removal from mechanical ventilation (C_R), medical-floor hospitalized post-ICU discharge (H_R), recovered from non-hospitalized infection (R), and discharged from hospital upon recovery (R_{HOSP}). Some compartments are broken down in sub-stages. For example, the exposed class is broken down into six sub-classes to reduce the coefficient of variation of the duration of the exposed period from 1.0 to 0.41. The justification for this particular parameter value[2] and all others can be found in the following table

https://github.com/bonilab/covid19-reopening-RI-MA-PA/blob/master/Nov2020/notes/summary.grouped_by_param.md (last accessed March 24 2022)

that summarizes the known studies from 2020 on clinical parameters of duration (how long a particular clinical state lasts for a patient) and probability (likelihood that a patient progresses to a more/less severe clinical state given a current clinical state). As a second example, time-to-death on mechanical ventilation is shorter than time-to-recovery on mechanical ventilation[3–6], and this is reflected in the model structure. eFigure 1 shows the model structure. The model is age-structured, thus every class is broken down into nine sub-compartments corresponding to 10-year age bands.

eFigure 1. Compartmental Model Diagram



eFigure 1. Compartmental diagram for ordinary differential equations (ODE) epidemic model used for inference. Each compartment is broken down into nine 10-year age bands. Individuals can be susceptible (*S*), exposed (*E*), asymptomatic (*A*), infected and symptomatic but not hospitalized (*I*), hospitalized in the acute stage of infection (H_A), in critical care during acute phase (C_A), on a ventilator (*V*), in critical care after being removed from mechanical ventilation (C_R), hospitalized and convalescing after being discharged from the ICU (H_R), recovered from non-hospitalized infection (*R*), recovered from an infection that required hospitalization (R_{HOSP}). Numbers in upper-right corner of each compartment show number of transitory states used to model that patient group. For example, there are six exposed classes, E_1 to E_6, each lasting approximately one day. Gray arrows indicate death. Green arrows show vaccination, but only the dashed green arrow moves individuals from one state to another.

Vaccination

The model is run from March 1 2020 to June 6 2021, and individuals begin to be vaccinated in the model on December 27 2020 in Rhode Island, December 30 2020 in Massachusetts, and February 10 2021 in Connecticut. The starting dates of vaccination campaigns in the model align with dates when the three states started to administer second doses of either the Moderna or Pfizer/BioNTech vaccines. The Connecticut vaccine data did not begin to be recorded until Feb 10 2021 (even though first doses were being distributed prior to January 15, in small numbers), but the CT model fit does not seem to show any irregularities during this early period. State vaccination data are available weekly and are age-structured (some age bands had to be converted to exact 10-year age groups), and these data are transformed into a daily time series through simple linear interpolation. During a model run, once per day, based on each state's data on second doses administered (or a single dose of the Johnson and Johnson vaccine), a number of individuals are chosen to be vaccinated in the model. An individual chosen for vaccination does not necessarily have to be in the *S* class as some individuals may not know that they were infected in the past or are currently infected; thus, individuals chosen for vaccination can come from any of the *S*, *E*, *A*, or *R* classes. In early 2021, individuals were encouraged to be vaccinated regardless of past vaccination status, although individuals with known past infections may have delayed their initial vaccinations; this is an assumption we make in our analysis, thus the total number of previously infected individuals that *also* received a SARS-CoV-2 vaccine during Jan-May 2021 represents the a minimum estimate for this overlap. Individuals who are infected but not showing symptoms can also be vaccinated in the model, and they simply continue with their regular course of infection. Equation (1) in the main text shows the fraction of vaccinees that would have been antibody-negative and virus-negative at time of vaccination.

Inference framework and likelihood model

The inference framework is presented in Section 3 of the Supplementary Materials to Wikle et al[1]. Briefly, the likelihood of the data is the product of the likelihood of SARS-CoV-2 incidence data and the likelihood of SARS-CoV-2 prevalence data. Incidence data – symptoms incidence, hospitalization incidence, hospital discharge incidence, and death incidence – are broken down into age groups and totals separately as the

sums across age groups do not always add up to the totals. Total incidence is modelled as a partially-observed process (of the differential equations model) with a negative binomial observation function, and age-structured incidence is modeled as a multinomial sample from the total incidence given the model's age-specific incidence trajectories. For days when no age data are available, the multinomial probability component is omitted. Exact likelihood equations are equations (S8) to (S12) in Wikle et al[1].

Current levels of hospitalization, ICU occupancy, and ventilator occupancy are modeled as normal distributions centered on the model's prediction (trajectory) of the number of patients in the hospital, ICU, and on a ventilator that day; the variance of each of these normal distributions is estimated. These normal likelihoods are only added into the full likelihood product every seven days as the three occupancy data streams are strongly auto-correlated.

Priors for parameters

A large number of parameters are estimated in the model, shown in eFigures 4 to 9. A time-varying reporting parameter ρ is estimated (Figure 2A, main text) to show the fraction of symptomatic COVID-19 cases that are captured by the health system (i.e. the proportion of symptomatic infected individuals who choose to seek care, are PCR-tested, and receive a true positive test result that is then sent to the state DOH). The reporting parameter ρ is modeled with an I-spline expansion with breakpoints set at April 1 2020, May 1 2020, July 1 2020, October 14 2020, and December 1 2020 to model an increasing symptomatic reporting rate over time. The spline breakpoints were chosen as we knew from state DOHs that testing access and reporting probability were low in March and possibly April 2020, and the other breakpoints allow for a gradual or rapid increase (depending on the data) of the reporting parameter from summer 2020 to the winter wave of 2020-2021. The reporting rate remains unchanged from December 1 2020 to May 31 2021. Cubic B-spline expansion with one basis function every seven days (total of 66 basis functions) was used to model the population-mixing parameter; see equation (S17) and blue lines in Figure 1 of Wikle et al[1].

eTable 1. Priors for Bayesian Inference

Parameter (uniform prior)	**Massachusetts**	**Rhode Island**	**Connecticut**
mean-time-vent (days)	[7.0, 14.0]	[7.0, 14.0]	[7.0, 14.0]
death-prob-home-60	[0.001, 0.2]	[0.001, 0.2]	[0.001, 0.2]
death-prob-home-70	[0.01, 0.3]	[0.01, 0.3]	[0.01, 0.3]
death-prob-home-80	[0.1, 0.4]	[0.1, 0.4]	[0.1, 0.4]
tv-dev-len-hospstay	[0.1, 2.0]	[0.1, 2.0]	[0.1, 2.0]
tv-dev-icu-frac_1	[0.01, 2.0]	[0.01, 1.5]	[0.4, 0.6]
tv-dev-icu-frac_2	[0.01, 2.0]	[0.01, 2.0]	[0.01, 2.0]
tv-dev-icu-frac_3	[0.01, 2.0]	[0.01, 2.0]	[0.01, 2.0]
tv-dev-icu-frac-endday_1	[110, 200] i.e. from April 19 2020 to July 18 2020	[130, 165] i.e. from May 9 2020 to June 13 2020	[140, 210] i.e. from May 19 2020 to July 28 2020
tv-dev-icu-frac-endday_2	[250, 380] i.e. from September 6 2020 to January 14 2021	[180, 360] i.e. from June 28 2020 to December 25 2020	[280, 360] i.e. from October 6 2020 to December 25 2020
prob-icu-vent	[0.4, 1.0]	[0.4, 1.0]	[0.4, 1.0]
dev-ventdeath-mid	[0.4, 1.5]	[0.4, 1.5]	[0.4, 1.5]
tv-hosp-frac-10	[0.001, 0.1]	[0.001, 0.1]	[0.001, 0.1]
tv-hosp-frac-20	[0.001, 0.1]	[0.001, 0.1]	[0.001, 0.1]
tv-hosp-frac-30	[0.005, 0.15]	[0.005, 0.15]	[0.005, 0.15]
tv-hosp-frac-40	[0.005, 0.15]	[0.005, 0.15]	[0.005, 0.15]
tv-hosp-frac-50	[0.01, 0.2]	[0.01, 0.2]	[0.01, 0.2]
tv-hosp-frac-60	[0.05, 0.2]	[0.05, 0.2]	[0.05, 0.2]
tv-hosp-frac-70	[0.1, 0.4]	[0.1, 0.4]	[0.1, 0.4]
tv-hosp-frac-80	[0.1, 0.4]	[0.1, 0.4]	[0.1, 0.4]
First set of age-specific contact rates (8 parameters: tv-contact-rate-10_1, …, tv-contact-rate-80_1)	[0.1, 10.0], identical range for all 8 parameters	[0.1, 10.0], identical range for all 8 parameters	[0.1, 10.0], identical range for all 8 parameters
Second set of age-specific contact rates (8 parameters: tv-contact-rate-10_2, …, tv-contact-rate-80_2)	[0.1, 10.0], identical range for all 8 parameters	[0.1, 10.0], identical range for all 8 parameters	[0.1, 10.0], identical range for all 8 parameters
Third set of age-specific contact rates (8 parameters: tv-contact-	[0.1, 10.0], identical range for all 8 parameters	[0.1, 10.0], identical range for all 8 parameters	[0.1, 10.0], identical range for all 8 parameters

rate-10_3, …, tv-contact-rate-80_3)			
Fourth set of age-specific contact rates (8 parameters: tv-contact-rate-10_4, …, tv-contact-rate-80_4)	[0.1, 10.0], identical range for all 8 parameters	NA	NA
tv-contact-rate-endday_1	[100, 190] i.e. from April 9 2020 to July 8 2020	[120, 190] i.e. from April 29 2020 to July 8 2020	[100, 190] i.e. from April 9 2020 to July 8 2020
tv-contact-rate-endday_2	[230, 305] i.e. from August 17 2020 to October 31 2020	[250, 410] i.e. from September 6 2020 to February 13 2021	[250, 390] i.e. from September 6 2020 to January 24 2021
tv-contact-rate-endday_3	[330, 420] i.e. from November 25 2020 to February 23 2021	NA	NA

Priors that differ between states are shown in purple.

The parameter "`mean-time-vent`" is the mean number of days a surviving patient spends on a ventilator. The parameter "`death-prob-home-nn`" is the probability that a patient in a particular age class dies of COVID-19 without being hospitalized; these parameters are necessary as positive patients in care in nursing homes were not classified as hospitalized even when infections were severe. Parameters with the word "`dev`" model a multiplicative deviation from a standard parameter. For example, "`tv-dev-len-hospstay`" is a scaling factor used to multiply the model's average 10.7 day hospital stay[7] (medical-floor, non-ICU). The "`dev-icu-frac`" parameters modify the age-specific probabilities of progression to ICU from Lewnard et al[7] (all probabilities are multiplied simultaneously, to keep the relative probabilities the same across ages) and they allow for inference on three separate severity periods during the 15-month epidemic (clinical practice improved during the course of the pandemic). The first period for Connecticut differs from all the others (prior set to [0.4-0.6]) because there were no ICU data for Connecticut until July 15 2020. The two "`endday`" parameters that follow give the priors for the breakpoints demarking the periods when clinical management in hospital improved; the priors set for these breakpoints are not identical because of the difficulty of fitting these particular parameters (see bottom right panels of eFigure 4). A

lower ICU admission fraction suggests that hospitalized patients have improved chances of recovery and a lower chance of death. The first changepoint was inferred as Jun 2 for RI, May 26 for MA, and Jun 5 for CT (medians from posteriors), and the second changepoints were inferred as Dec 10 for RI, Sep 12 for MA, and Nov 6 for CT (see bottom right panels of eFigure 4).

The parameter "`prob-icu-vent`" describes the probability of progressing from ICU care to mechanical ventilation, and the "`dev-ventdeath-mid`" parameter allows for flexible fitting of death probability for the 40-70 age group where uncertainty was the greatest. The "`hosp-frac`" parameters give the age-specific probabilities of progressing from symptomatic infection to hospitalization. Age-specific relative contact rates (or mixing rates) have priors of [0.1, 10.0] where 1.0 is the contact rate for the 0-9 age group (the reference group). Connecticut and Rhode Island have three different periods of age-mixing patterns, while Massachusetts had four periods (based on lower BIC and better visual fit). These three or four periods are separated by the "`endday`" parameters at the bottom of eTable 1, whose priors again are slightly different due to the difficulty of fitting these breakpoints.

Posterior distributions of all parameters that were fit are shown in eFigures 4 to 9.

eAppendix 2. Data Streams

Collection of Massachusetts and Rhode Island data streams

Data streams for MA and RI were collected as outlined in Wikle et al[1]. In addition, age-structured cumulative hospitalization incidence was added for MA as this data stream was not available for our previous two analyses[1,8]. Details available in the supplementary materials file available at this link:

https://www.science.org/doi/suppl/10.1126/sciadv.abf9868/suppl_file/sciadv.abf9868_sm.pdf

Aggregation and cleaning of Connecticut data streams

Inference framework for Connecticut was based on the same eleven data streams as for RI and MA: (1) cumulative confirmed cases, (2) cumulative confirmed cases by age, (3) cumulative hospitalized cases, (4) cumulative hospitalized cases by age, (5) number of patients currently hospitalized, (6) number of patients currently in ICU, (7) number of patients currently on mechanical ventilation, (8) cumulative deaths, (9) cumulative deaths by age, (10) cumulative hospital deaths, (11) cumulative hospital discharges. Remember that age-structured data streams (*a*) do not always add up to the totals data stream and (*b*) normally have substantial missingness.

Data streams (1), (2), (5), (8), and (9) were collected from daily test results from the Connecticut Department of Public Health (CT DPH) (https://data.ct.gov/Health-and-Human-Services/COVID-19-daily-and-cumulative-cases-deaths-and-tes/5dch-cm68). Cases were defined as individuals with laboratory-confirmed positive COVID-19 tests. Age-stratified cumulative cases and deaths were obtained from the CT DPH website (https://data.ct.gov/Health-and-Human-Services/COVID-19-Cases-and-Deaths-by-Age-Group/ypz6-8qyf). Currently hospitalized patient counts were collected from the daily reports of CT DPH (https://data.ct.gov/Health-and-Human-Services/COVID-19-Tests-Cases-Hospitalizations-and-Deaths-S/rf3k-f8fg).

The remaining data streams were collected from other sources.

Data streams (3) and (4) were obtained from the CDC as there were no available total and age-stratified cumulative hospitalized case numbers available from CT DPH. Specifically, these data streams were calculated from the cumulative hospitalization rates from COVID-NET (https://gis.cdc.gov/grasp/COVIDNet/COVID19_3.html) using the population estimates from 2019 US census (https://www.census.gov/quickfacts/fact/table/US/PST045219). The age groups of cumulative hospitalizations from COVID-NET are 0-4, 5-17, 18-29, 30-39, 40-49, 50-64, 65-74, 75-84, and 85+. These age groups were re-binned to conform with the 10-year age bands used in our analysis. For age <30, we assumed that each age group had the same probability of being hospitalized, thus the age bands were re-binned assuming a uniform distribution of hospitalization in 1-year age bands. For age >50, we assumed that the age distribution of the CT hospitalized population followed the same pattern as Rhode Island. Thus, the hospitalization numbers in CT were re-binned to preserve the relative ratios of hospitalization among the 50-59, 60-69, 70-79, and 80+ age groups.

Data stream (6), the current number of patients in the ICU, was collected from the hospital utilization report from the Department of Health and Human Services (https://healthdata.gov/Hospital/COVID-19-Reported-Patient-Impact-and-Hospital-Capa/g62h-syeh), which includes the number of adult patients currently hospitalized in an ICU beds. These data were available from July 15 2020 forward.

Data stream (7), the number of patients on ventilators, was not available.

Data stream (10), cumulative hospital deaths, was not available.

Data stream (11), cumulative hospital discharges, was available from the COVID Tracking Project (https://covidtracking.com/data/state/connecticut). But this data stream was only available weekly, and only

from 6/4/2020 to 10/22/2020, and was thus not used in the data fitting. More recent data (Jan 2022) have this data stream available from 5/1/2020 to 10/22/2020.

Vaccination Data in Connecticut

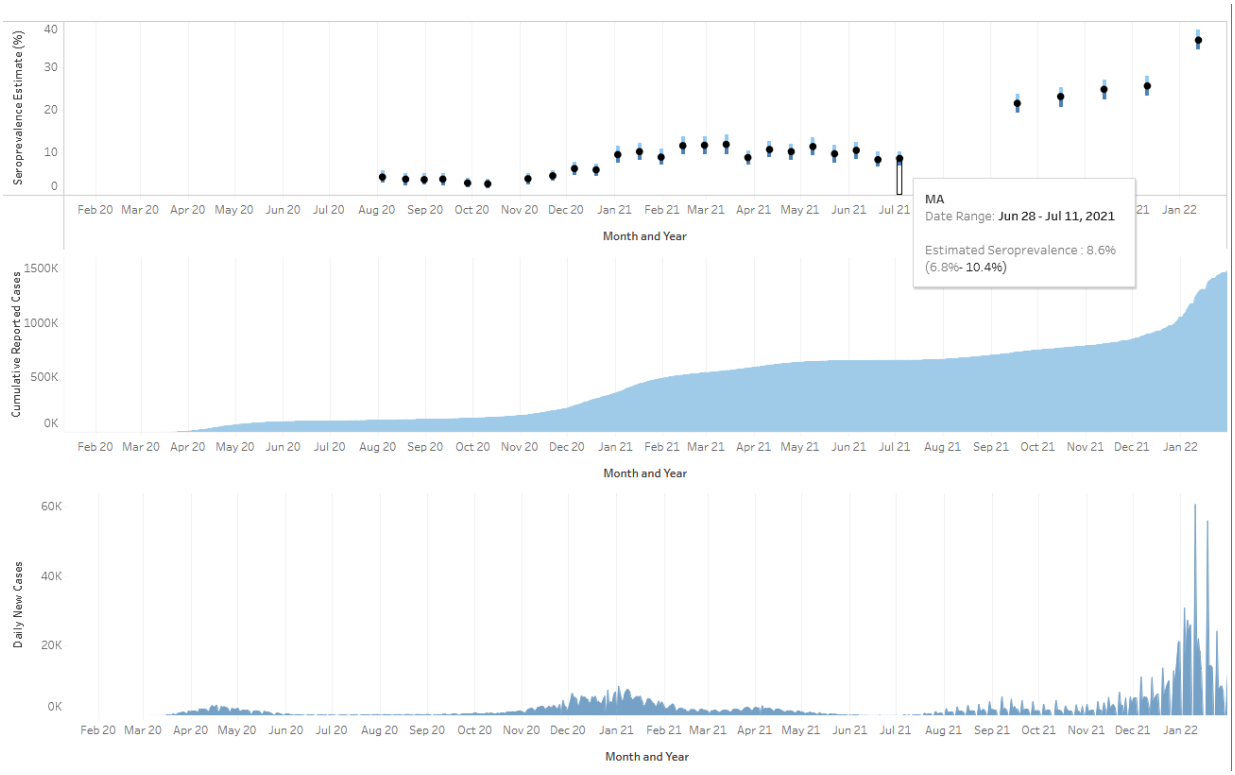
Total (https://data.ct.gov/Health-and-Human-Services/COVID-19-Vaccination-Status-by-Residence-in-a-SVI-/tttv-egb7) and age-stratified fully vaccinated population numbers (https://data.ct.gov/Health-and-Human-Services/COVID-19-Vaccinations-by-Age-Group/vjim-iz5e) were collected from the CT DPH website. A person is considered fully vaccinated if they received two doses of the Pfizer or Moderna vaccines or one dose of the Johnson & Johnson vaccine.

eAppendix 3. Interpretation of Seroprevalence Data

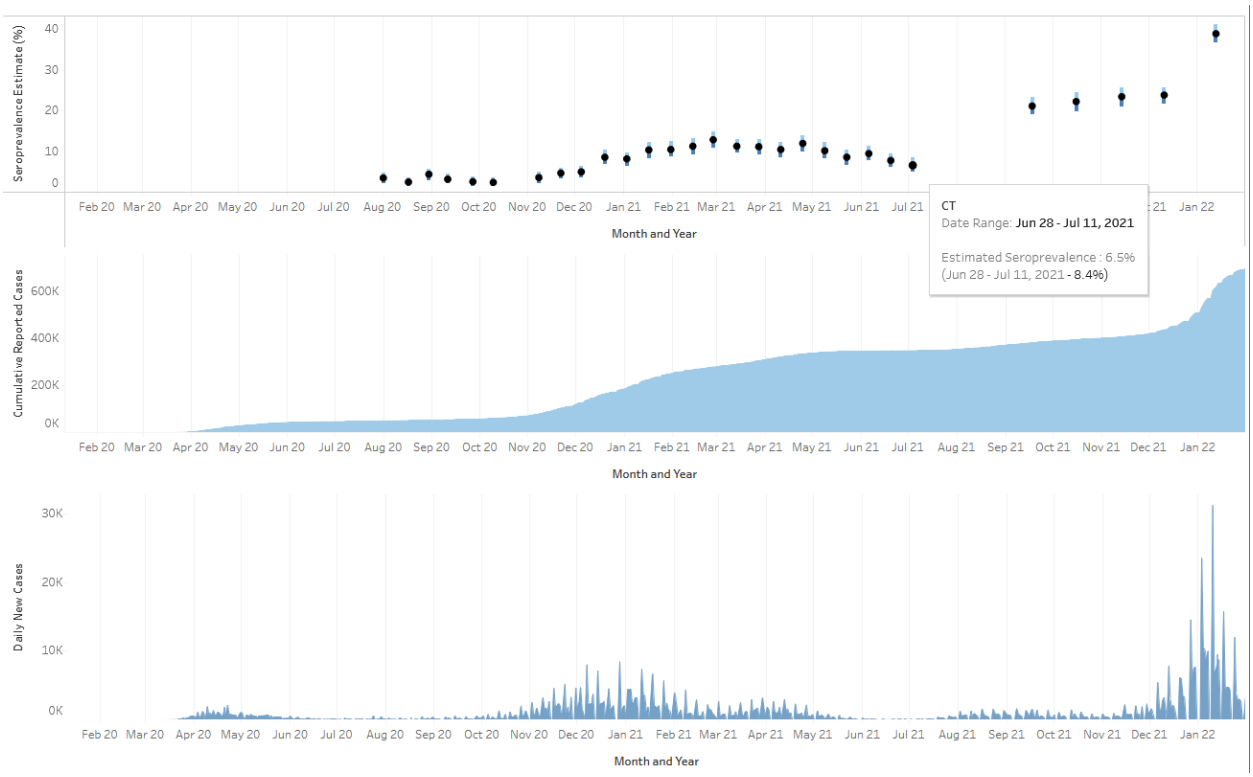
Comparison of our attack-rate estimates to CDC seroprevalence data reveals an important general gap in seroepidemiology in that there is no precise or useful measure of 'recent seroprevalence'. Antibodies to SARS-CoV-2 wane detectably over a period of 3-7 months, depending on the assay and antigen used[9–13]. For an epidemic analysis over 15 months, it is necessary to account for the effects of antibody waning.

The commercial-lab survey results reported by CDC (https://covid.cdc.gov/covid-data-tracker/#national-lab), using nucleocapsid antigen detection only thus excluding vaccinees, show 6% to 10% seroprevalence in RI, MA, and CT through June 2021. These are much lower than the 26% to 42% estimates we report.

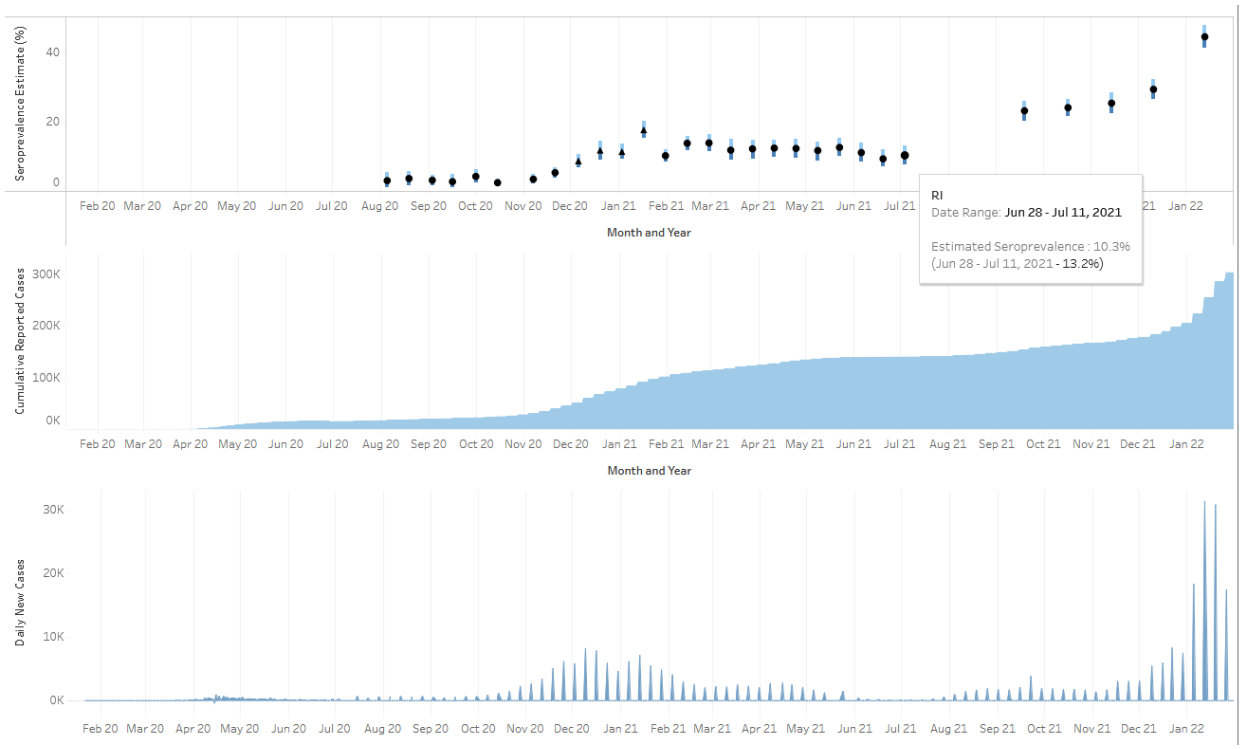
Screenshots below taken March 26 2022 for Massachusetts



Connecticut



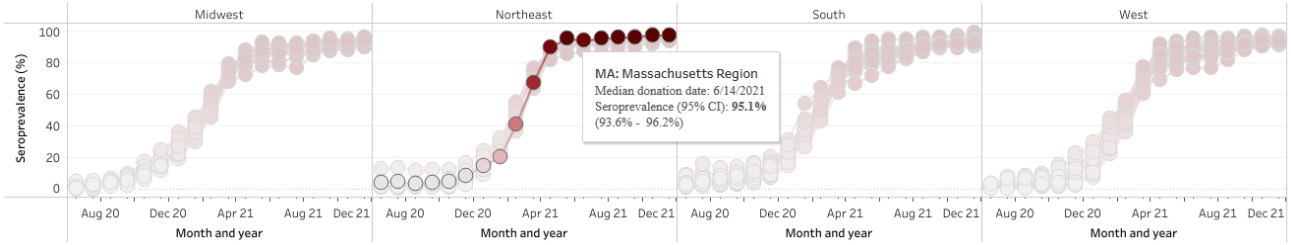
and Rhode Island



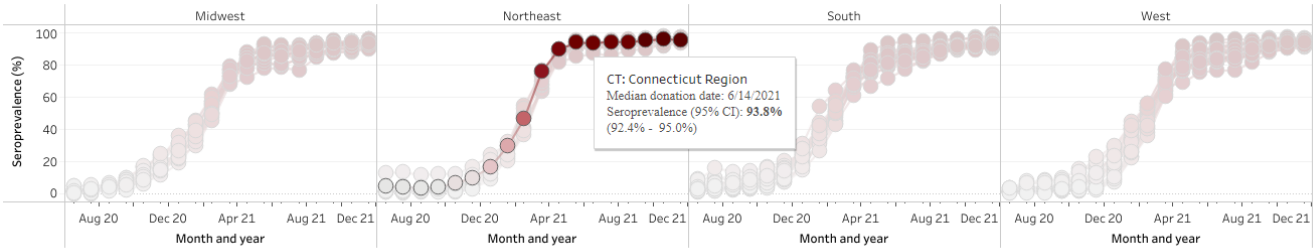
The flat/declining seroprevalence estimates from Feb 2021 to June 2021 in these figures show that waning of antibodies was affecting the general-population estimates by introducing a downward bias into what we would want from a cumulative seroprevalence estimate. Each state reported tens of thousands of cases during this period, so the seroprevalence could not possibly have remained constant. The June 2021 estimates on the previous pages are much more accurately described as 'recent attack rate' or 'recent seroincidence', but there is no indication of how much of the recent past this estimate includes.

The CDC blood-donor surveys (https://covid.cdc.gov/covid-data-tracker/#nationwide-blood-donor-seroprevalence) use Spike antigen and thus present an estimate combining past infections and vaccinees. These June 2021 seroprevalence estimates range from 91% to 95% for MA, CT, and RI. The Jones et al[14] paper has May 2021 estimates at >85%.

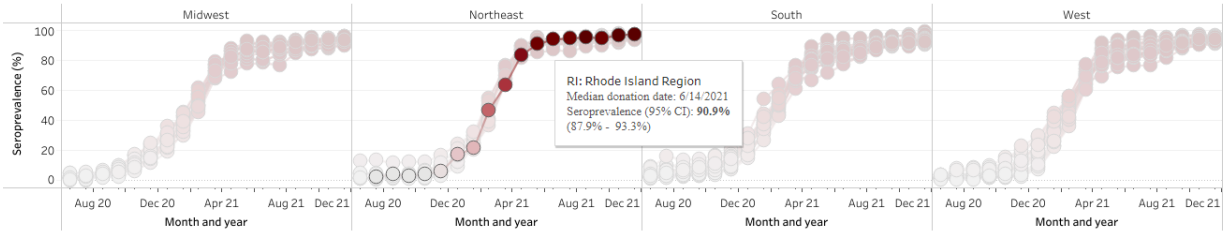
CDC screenshots below taken March 26 2022, for Massachusetts



Connecticut



and Rhode Island



Between 47% and 53% of each state's population was vaccinated by June 2021, thus vaccination numbers cannot make up for the discrepancy between the nucleocapsid (~10%) and Spike (>90%) seroprevalence estimates. It is possible that the Spike estimates are correct, but this is incompatible with our modeling analysis (with estimates between 64% and 73%), other modeling analyses[15,16] that place the infections-to-cases ratio at around 2.0 to 6.0, and the rapid rise of the Delta variant in late July 2021 in New England. The high Spike seroprevalence estimates may be influenced by a positive correlation between being a blood donor and vaccination uptake.

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eTable 2. Demographics of Confirmed COVID-19 Cases

age bracket	**Rhode Island**	**Connecticut**	**Massachusetts**
0-9	8344 (5.9%)	20,017 (6.3%)	126,824 (17.9%)
10-19	16,770 (11.8%)	37,685 (11.9%)	
20-29	27,603 (19.4%)	54,631 (17.2%)	133,296 (18.8%)
30-39	22,330 (15.7%)	49,058 (15.4%)	112,906 (15.9%)
40-49	18,712 (13.1%)	44,547 (14.0%)	96.435 (13.6%)
50-59	20,418 (14.3%)	48,075 (15.1%)	101,536 (14.3%)
60-69	14,254 (10.0%)	32,212 (10.1%)	69,170 (9.8%)
70-79	7231 (5.1%)	16,604 (5.2%)	35,407 (5.0%)
80+	6860 (4.8%)	15,085 (4.7%)	33,263 (4.7%)

Numbers (% of total) of COVID-19 cases with age information reported to state DOHs through late May or early June 2021 (June 5 for Rhode Island, June 4 for Connecticut, May 31 for Massachusetts). Massachusetts used a combined 0-19 age bracket.

eTable 3. Attack Rate Estimates from March 2020 to May 2021

Date	**Rhode Island**	**Connecticut**	**Massachusetts**
Mar 31 2020	1.17% (1.08% - 1.27%)	1.68% (1.55% - 1.84%)	0.85% (0.76% - 0.94%)
Apr 30 2020	4.04% (3.84% - 4.26%)	4.51% (4.30% - 4.76%)	2.49% (2.27% - 2.71%)
May 31 2020	5.72% (5.45% - 6.00%)	5.45% (5.21% - 5.73%)	3.59% (3.31% - 3.86%)
Jun 30 2020	6.51% (6.23% - 6.83%)	5.77% (5.53% - 6.05%)	4.13% (3.82% - 4.41%)
Jul 31 2020	7.56% (7.25% - 7.91%)	6.07% (5.82% - 6.35%)	4.67% (4.33% - 4.99%)
Aug 31 2020	8.62% (8.28% - 8.99%)	6.37% (6.13% - 6.65%)	5.24% (4.87% - 5.60%)
Sep 30 2020	10.03% (9.65% - 10.44%)	6.94% (6.68% - 7.25%)	6.08% (5.69% - 6.49%)
Oct 31 2020	13.19% (12.71% - 13.74%)	8.82% (8.50% - 9.23%)	7.65% (7.19% - 8.11%)
Nov 30 2020	19.43% (18.77% - 20.13%)	12.67% (12.35% - 13.04%)	11.18% (10.66% - 11.76%)
Dec 31 2020	25.57% (24.74% - 26.41%)	16.50% (16.19% - 16.90%)	16.25% (15.63% - 16.96%)
Jan 31 2021	30.24% (29.29% - 31.19%)	19.48% (19.16% - 19.93%)	20.48% (19.72% - 21.40%)
Feb 28 2021	33.29% (32.28% - 34.37%)	20.99% (20.68% - 21.44%)	22.33% (21.58% - 23.24%)
Mar 31 2021	36.51% (35.42% - 37.64%)	23.18% (22.86% - 23.68%)	24.74% (23.97% - 25.68%)
Apr 30 2021	40.25% (39.14% - 41.48%)	25.24% (24.91% - 25.76%)	27.21% (26.39% - 28.24%)
May 31 2021	41.51% (40.44% - 42.66%)	25.77% (25.45% - 26.29%)	27.96% (27.13% - 29.01%)

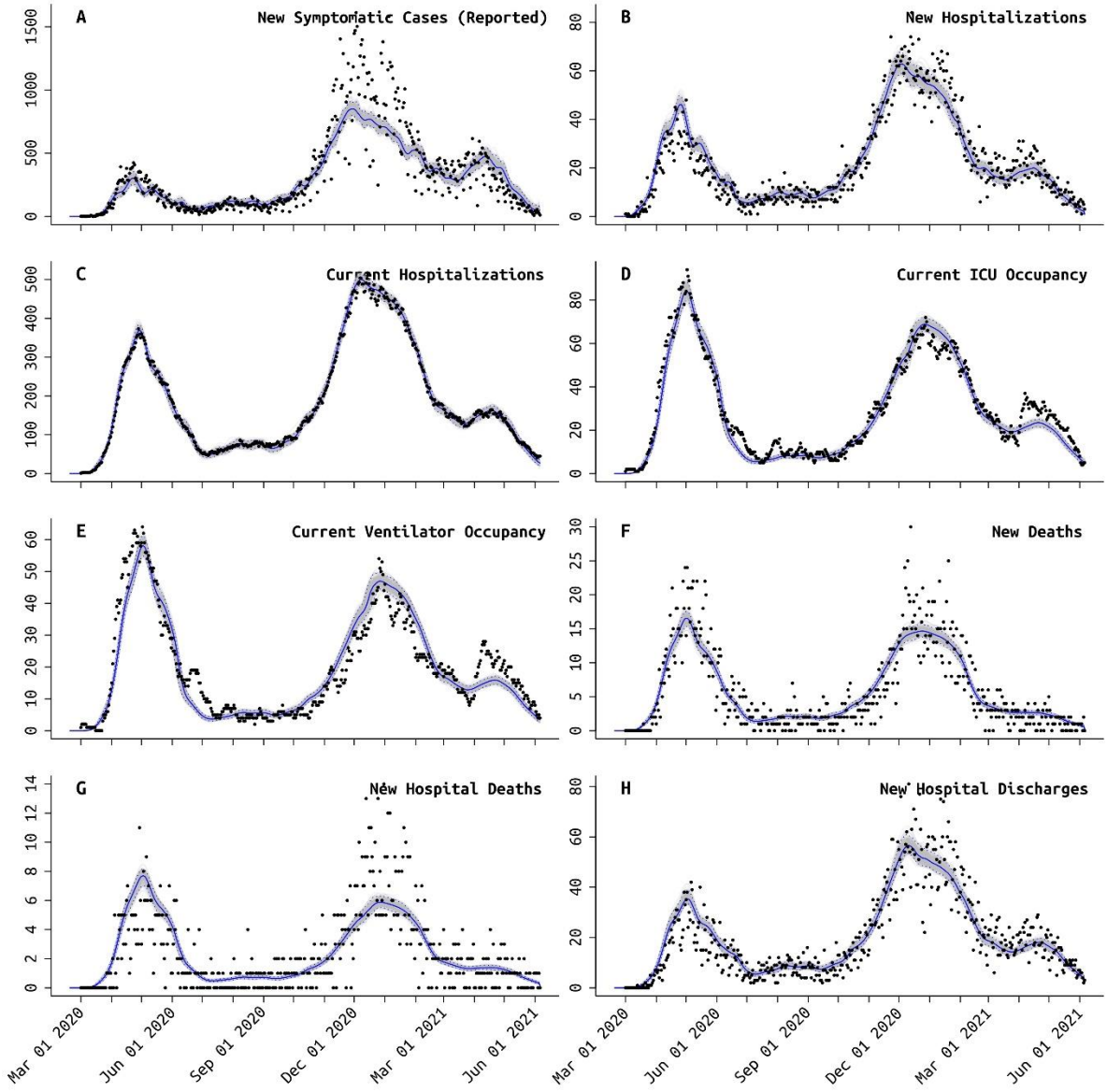
Median (95% credible interval) monthly attack rate estimates for Rhode Island, Connecticut, and Massachusetts from March 2020 to May 2021. These are shown as blue lines in Figure 4.

eTable 4. Population Immunity Estimates from March 2020 to May 2021

Date	**Rhode Island**	**Connecticut**	**Massachusetts**
Mar 31 2020	1.17% (1.08% - 1.27%)	1.68% (1.55% - 1.84%)	0.85% (0.76% - 0.94%)
Apr 30 2020	4.04% (3.84% - 4.26%)	4.51% (4.30% - 4.76%)	2.49% (2.27% - 2.71%)
May 31 2020	5.72% (5.45% - 6.00%)	5.45% (5.21% - 5.73%)	3.59% (3.31% - 3.86%)
Jun 30 2020	6.51% (6.23% - 6.83%)	5.77% (5.53% - 6.05%)	4.13% (3.82% - 4.41%)
Jul 31 2020	7.56% (7.25% - 7.91%)	6.07% (5.82% - 6.35%)	4.67% (4.33% - 4.99%)
Aug 31 2020	8.62% (8.28% - 8.99%)	6.37% (6.13% - 6.65%)	5.24% (4.87% - 5.60%)
Sep 30 2020	10.03% (9.65% - 10.44%)	6.94% (6.68% - 7.25%)	6.08% (5.69% - 6.49%)
Oct 31 2020	13.19% (12.71% - 13.74%)	8.82% (8.50% - 9.23%)	7.65% (7.19% - 8.11%)
Nov 30 2020	19.43% (18.77% - 20.13%)	12.67% (12.35% - 13.04%)	11.18% (10.66% - 11.76%)
Dec 31 2020	25.57% (24.74% - 26.41%)	16.50% (16.19% - 16.90%)	16.25% (15.63% - 16.96%)
Jan 31 2021	32.21% (31.28% - 33.13%)	19.48% (19.16% - 19.93%)	22.09% (21.34% - 22.99%)
Feb 28 2021	38.70% (37.76% - 39.71%)	29.04% (28.75% - 29.46%)	28.84% (28.14% - 29.69%)
Mar 31 2021	53.28% (52.39% - 54.22%)	40.04% (39.76% - 40.46%)	40.87% (40.21% - 41.66%)
Apr 30 2021	65.78% (65.03% - 66.67%)	54.55% (54.33% - 54.92%)	55.45% (54.86% - 56.17%)
May 31 2021	73.40% (72.89% - 74.08%)	64.13% (63.95% - 64.42%)	66.33% (65.87% - 66.90%)

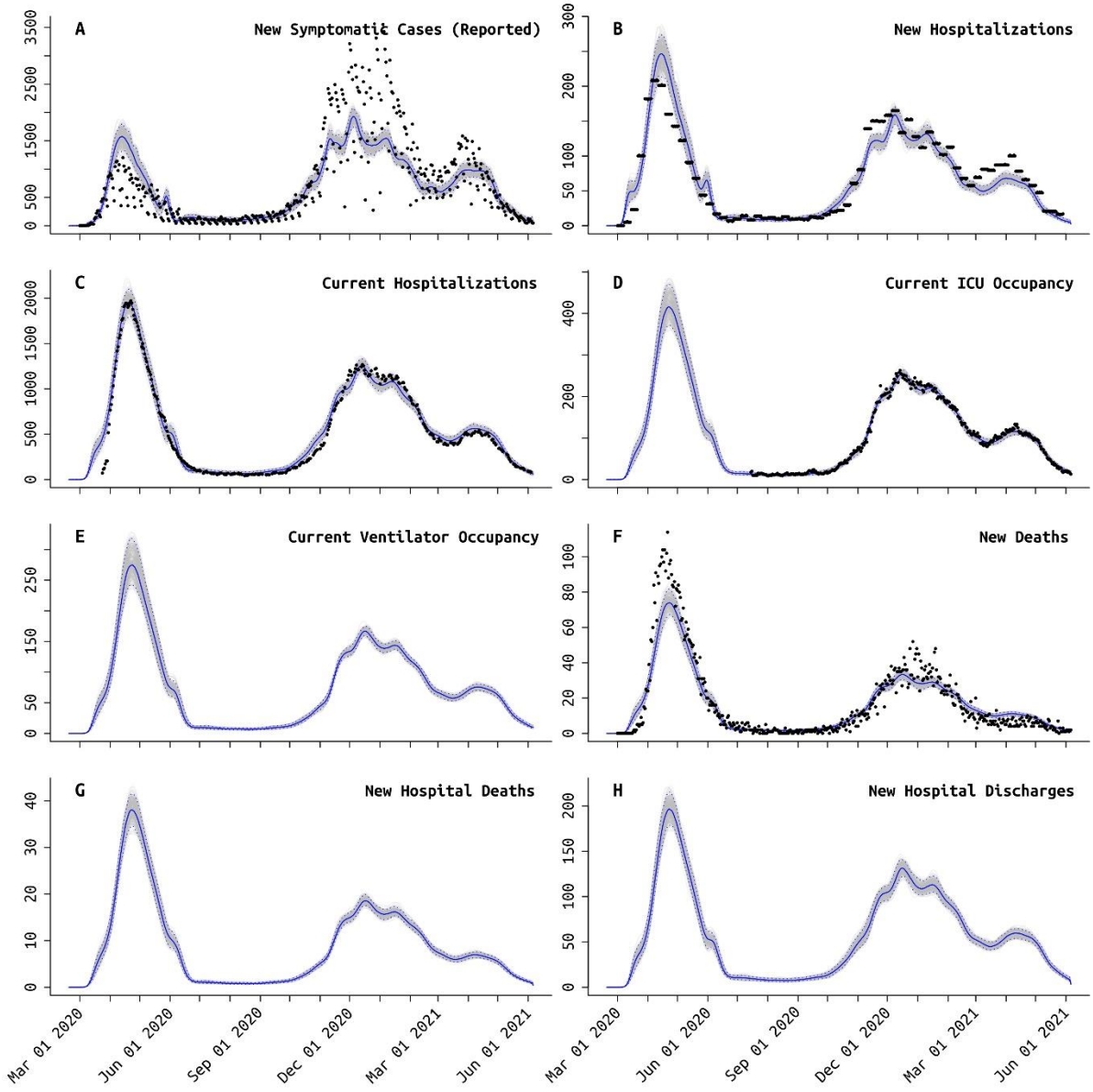
Median (95% credible interval) monthly population immunity estimates for Rhode Island, Connecticut, and Massachusetts from March 2020 to May 2021. These are shown as green lines in Figure 4.

eFigure 2. Rhode Island Model Fit



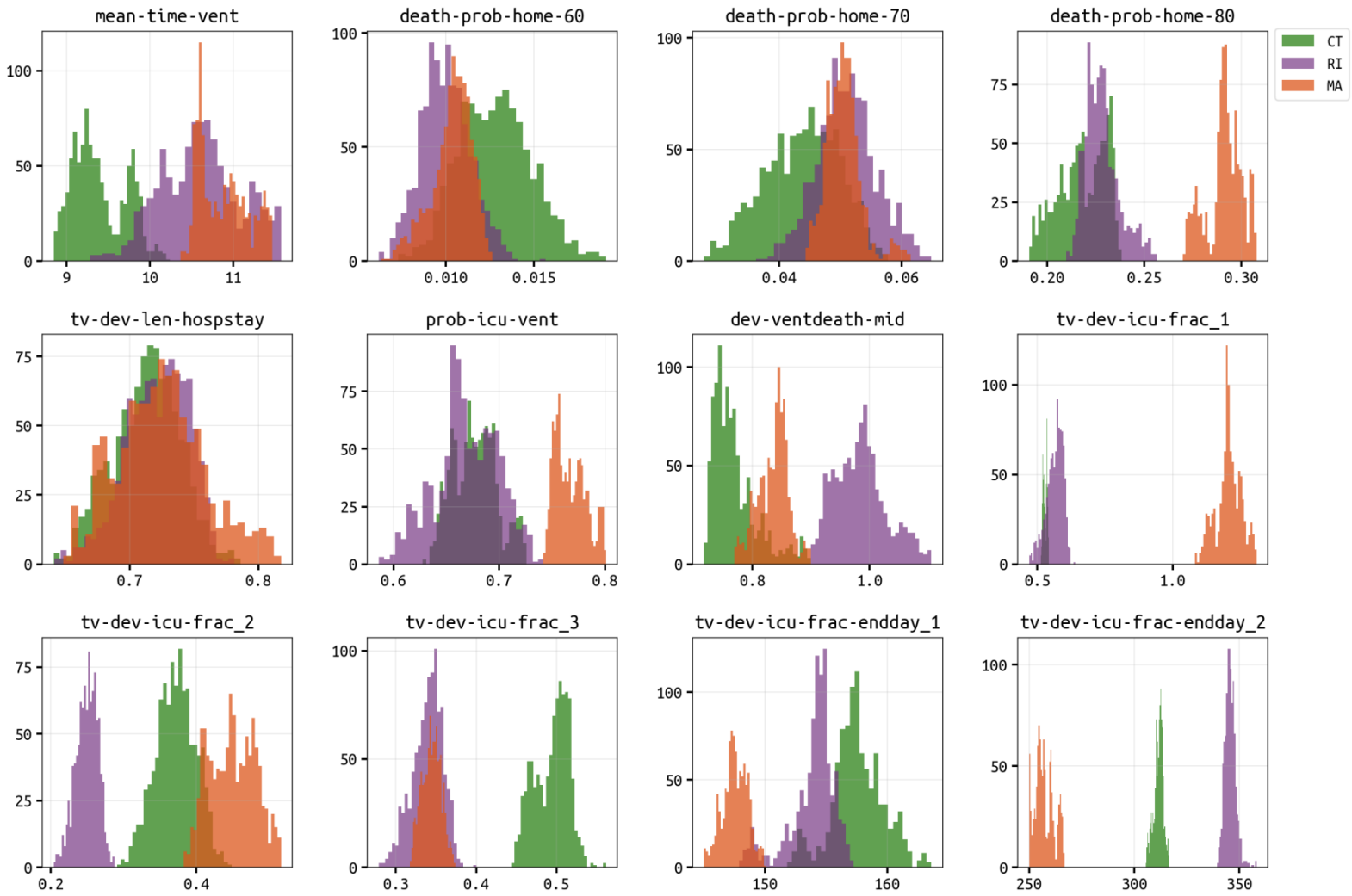
eFigure 2. Rhode Island fit of model to data. Panels **A**, **B**, and **F** also have age-structured data streams, making a total of 11 data streams. Black dots are absolute daily counts. Blue line is model median from the posterior, and gray bands show 95% credible region.

eFigure 3. Connecticut Model Fit



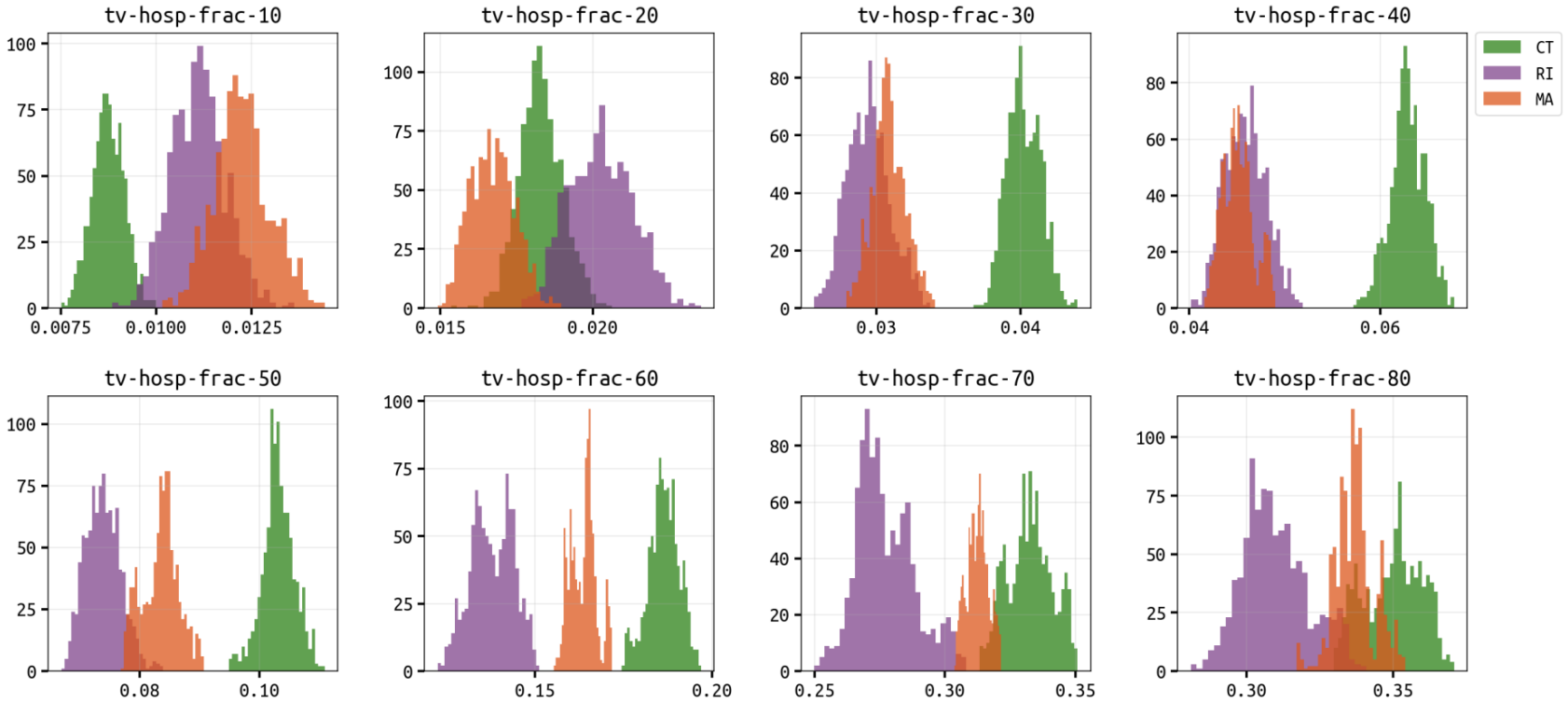
eFigure 3. Connecticut fit of model to data. Panels **A**, **B**, and **F** also have age-structured data streams. Hospital discharge data, death data separated by in/out of hospital, and ventilated patient counts were not available in Connecticut. Black dots are absolute daily counts. Blue line is model median from the posterior, and gray bands show 95% credible region.

eFigure 4. Posterior Distributions



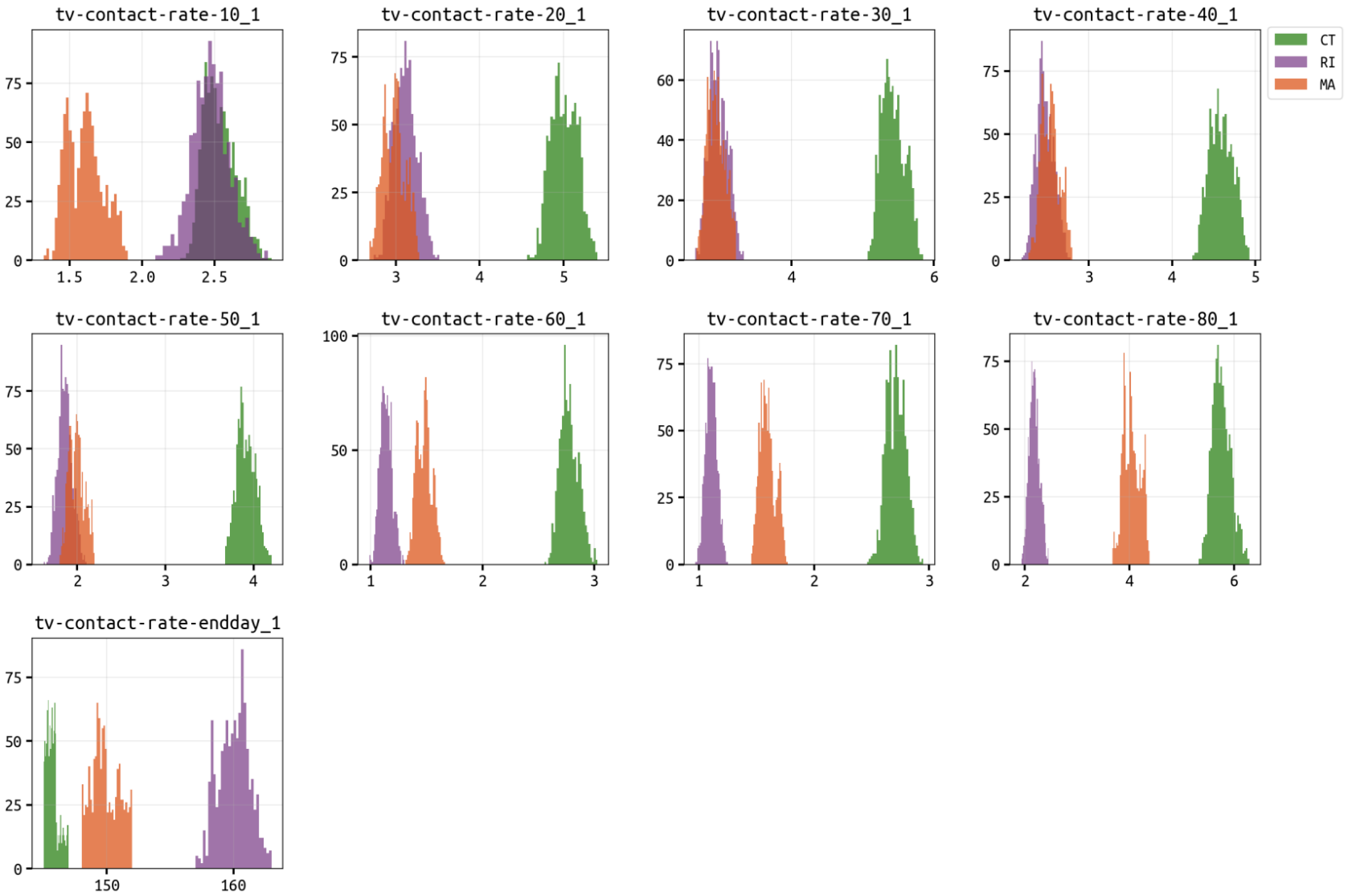
eFigure 4. Panels show posterior distributions for mean number of days a patient spends on a ventilator (**mean-time-vent**); age-specific probability of death in ten-year age bands for symptomatic patients outside hospital settings (e.g. **death-prob-home-60** for the 60-69 age group); the average length of non-ICU hospital stay (**tv-dev-len-hospstay**, multiply by 10.8 days); probability of progression from non-ventilated to ventilated status in the ICU (**prob-icu-vent**); deviation from expected mortality rate for 40-70 year-olds on ventilators (**dev-ventdeath-mid**); for three periods of the epidemic, the relative probability of ICU admission for hospitalized patients (**tv-dev-icu-frac_1**, tv-**dev-icu-frac_2**, **tv-dev-icu-frac_3**); the end-days of the first two periods with aforementioned ICU admission probabilities (**tv-dev-icu-endday_1**, **tv-dev-icu-endday_2**, day 150 is May 30 2020, day 300 is Oct 26 2020).

eFigure 5. Posterior Distributions



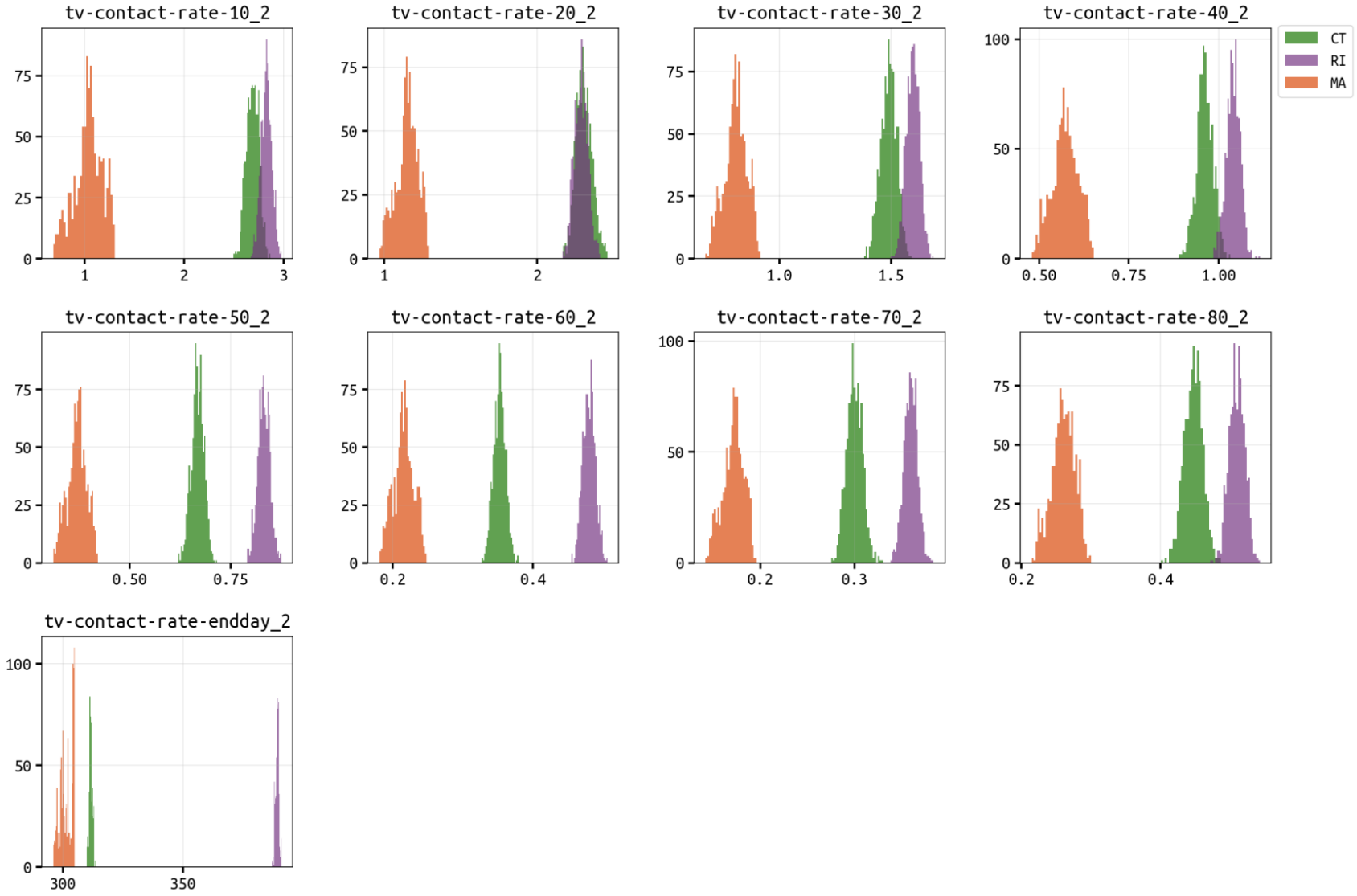
eFigure 5. Panels show posterior distributions for the probability of hospitalization for a symptomatic infection of SARS-CoV-2, by 10-year age band, starting at 10-19, 20-29, through to the 80+ age group. The 0-9 age group is assumed to have the same probability of hospitalization as the 10-19 age group.

eFigure 6. Posterior Distributions



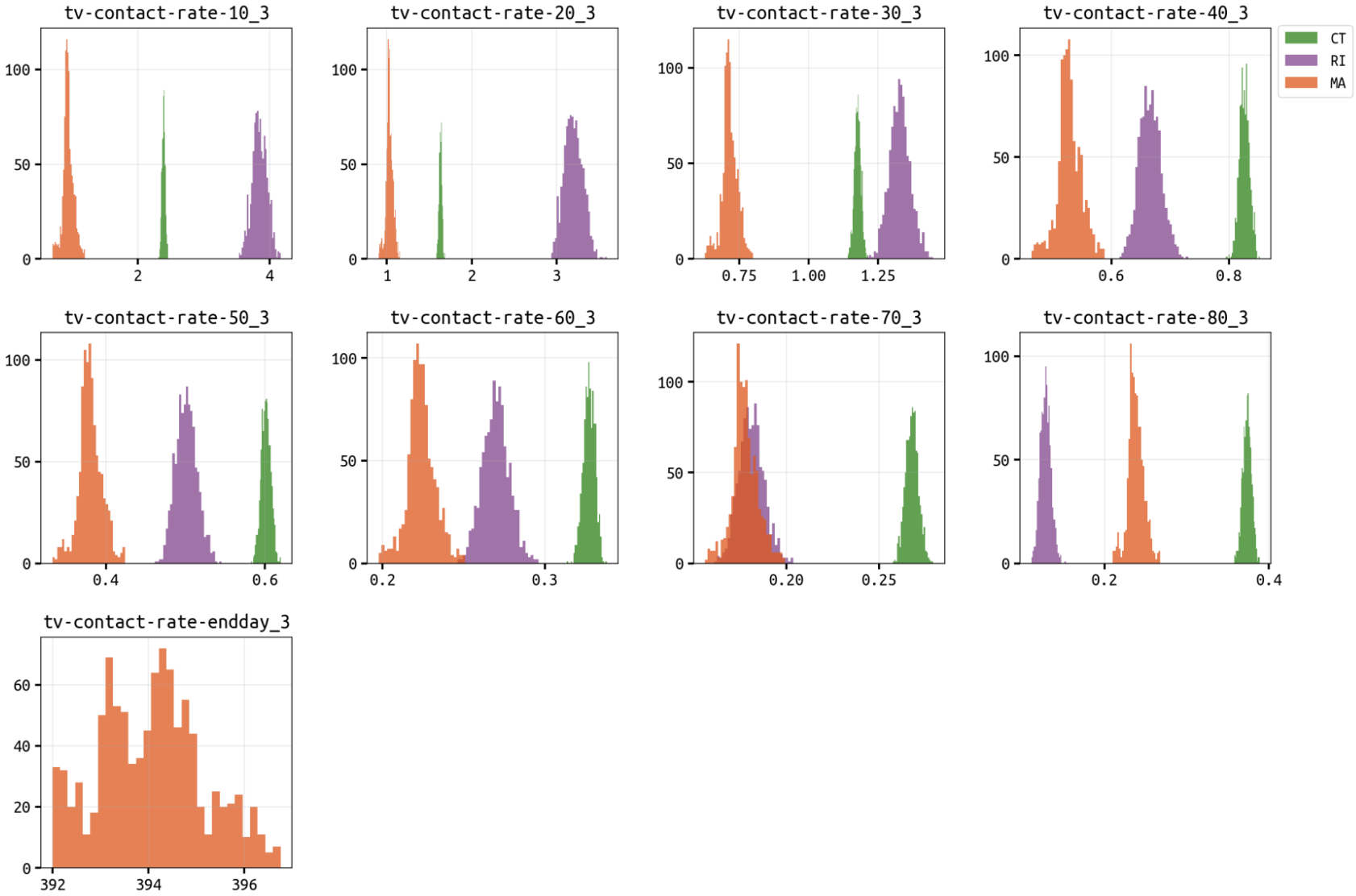
eFigure 6. Panels show posterior distributions for relative "transmission-capable contact rate" for the first period of inference which ends at **tv-contact-rate-endday_1** (posteriors shown in bottom panel; day 150 is May 30 2020). Contact rates are broken down by age group (10-19, 20-29 to 80+) and are all presented as relative to the contact rate of the 0-9 age group.

eFigure 7. Posterior Distributions



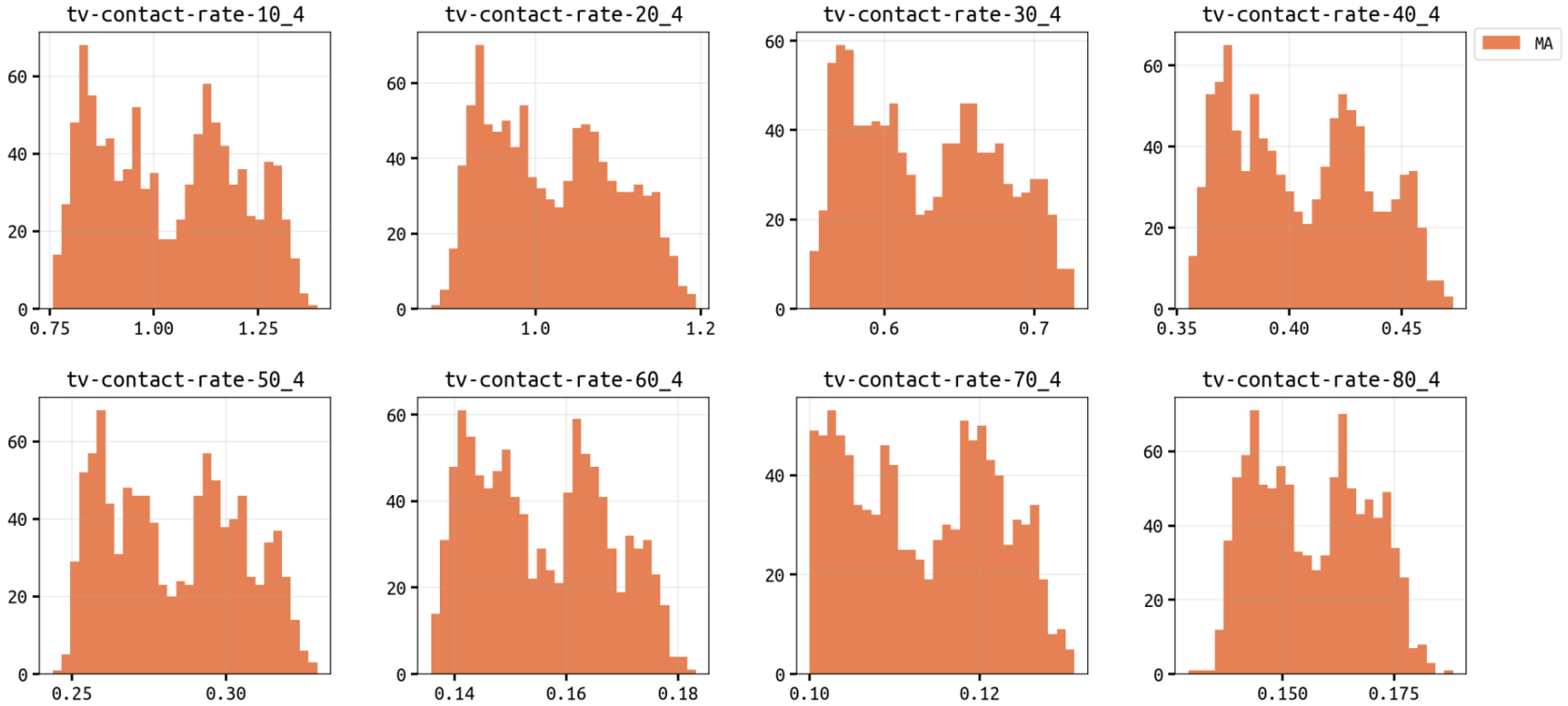
eFigure 7. Panels show posterior distributions for relative "transmission-capable contact rate" for the second period of inference which ends at **tv-contact-rate-endday_2** (posteriors shown in bottom panel; day 300 is Oct 26 2020). Contact rates are broken down by age group (10-19, 20-29 to 80+) and are all presented as relative to the contact rate of the 0-9 age group.

eFigure 8. Posterior Distributions



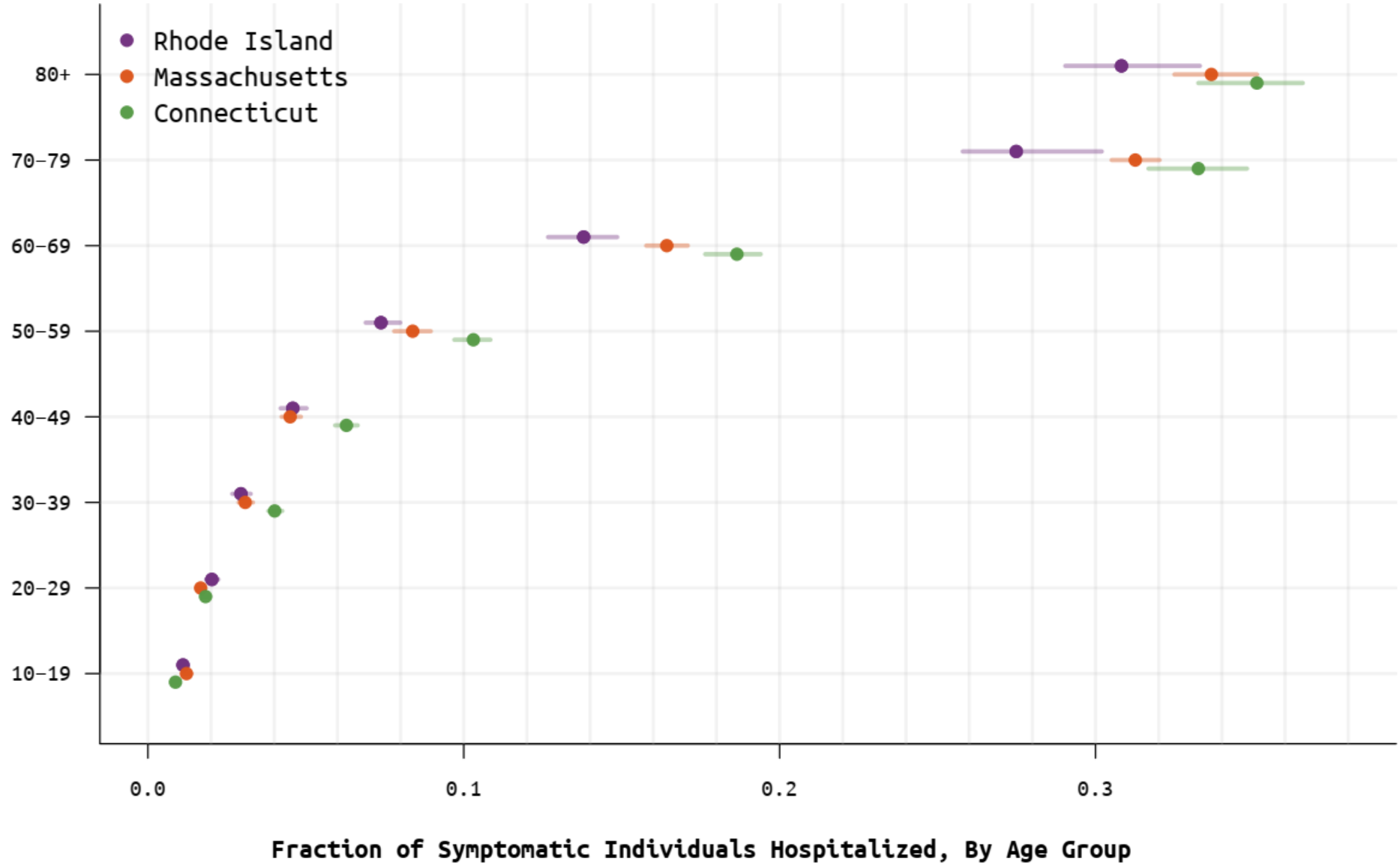
eFigure 8. Panels show posterior distributions for relative "transmission-capable contact rate" for the third period of inference which ends at **tv-contact-rate-endday_3** for Massachusetts (posterior shown in bottom panel; day 394 is Jan 28 2021) or ends on May 31 2021 for Rhode Island and Connecticut. Contact rates are broken down by age group (10-19, 20-29 to 80+) and are all presented as relative to the contact rate of the 0-9 age group.

eFigure 9. Posterior Distributions



eFigure 9. Panels show posterior distributions for relative "transmission-capable contact rate" for the fourth period of inference which ends was only used for the Massachusetts inference (based on DIC and visual fit). Contact rates are broken down by age group (10-19, 20-29 to 80+) and are all presented as relative to the contact rate of the 0-9 age group.

eFigure 10. Alternate Visualization for Hospitalization Probability



eFigure 10. Age-specific probability (*x*-axis) of hospitalization by age group (*y*-axis). Dots are medians and bars represent 95% credible intervals. Colors represent the three different states. This visualization is simply an alternate view of the posteriors presented in eFigure 5.