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Modelling the Interplay between Responsive Individual Vaccination Decisions and the Spread of SARS-CoV-2

by

Karina Wallrafen-Sam
Master of Science in Public Health

Epidemiology

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Samuel M. Jenness, PhD
Committee Chair

# Modelling the Interplay between Responsive Individual Vaccination Decisions and the Spread of SARS-CoV-2

by

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Bachelor of Science in Applied Mathematics
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2019

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**Abstract**

Modelling the Interplay between Responsive Individual Vaccination Decisions and the Spread of SARS-CoV-2

By Karina Wallrafen-Sam

**Background.** The uptake of primary and booster vaccinations against SARS-CoV-2 infection remains low despite high vaccine effectiveness. Vaccine hesitancy is a major barrier to higher uptake, but it is unclear whether modifying hesitancy could result in substantial prevention benefits. Mathematical models of disease transmission that represent decision-making psychology can provide insight into the potential effects of different interventions against vaccine hesitancy in the context of the ongoing COVID-19 pandemic.

**Methods.** We coupled a network-based mathematical model of SARS-CoV-2 transmission with a social-psychological vaccination decision-making process in which vaccine side effects and breakthrough (i.e., post-vaccination) infections could "nudge" agents towards vaccine resistance while spikes in COVID-19 hospitalizations could nudge them towards vaccine willingness. This model was parameterized and calibrated to represent the COVID-19 epidemic in the state of Georgia, USA from January 2021 to August 2022. We modelled various intervention scenarios in which increases to the probability of resistant-to-willing attitude switches were combined with decreases to the probability of willing-to-resistant switches. We compared cumulative vaccine doses administered, SARS-CoV-2 incidence, and COVID-related deaths across scenarios.

**Results.** Increasing the probability that a spike in hospitalized prevalence would prompt vaccine resistant persons to vaccinate and decreasing the probability that breakthrough infections would prompt vaccine willing persons to forgo further vaccination both increased the intermediate outcome of cumulative vaccine doses administered by as much as 1'632.0 doses (50% SI: (1'358.5, 1'854.5)), with the former probability having more of an impact than the latter. However, this additional vaccine coverage built up too slowly to avert a non-negligible number of infections or deaths within our model timeframe. The minimum number of infections across scenarios was 67'111.7 per 100'000 person-years (50% SI: (66'344.0, 67'976.6)), corresponding to only 634.7 (50% SI: (-230.2, 1'402.4)) infections averted per 100'000 person-years.

**Conclusions.** Reactive interventions may have only a limited ability to avert SARS-CoV-2 infections in the short term. This suggests that attention should be paid to formulating vaccine promotion interventions that anticipate the case curve instead of reacting to it. Our findings also highlight the importance of addressing baseline vaccine unwillingness to reduce the proportion of the population that is entirely vaccine-naïve.

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## BACKGROUND

The worldwide spread of SARS-CoV-2, the virus which causes COVID-19 disease, has already become one of the defining health events of the 21st century, and one of the most impactful pharmaceutical interventions to date against this outbreak has been the development and distribution of highly effective vaccines. The COVID-19 vaccine rollout in the United States began in late 2020 with a two-dose primary series, before waning immunity and decreased effectiveness against novel SARS-CoV-2 strains prompted the development of three booster vaccinations: two monovalent boosters, the latter of which was recommended for certain populations only, and an updated bivalent booster that became available in late 2022 and is currently recommended for anyone who received their last dose at least two months ago.[1] Although these vaccines have been widely available in the United States for the past two years, only about 69% of the eligible U.S. population had completed the primary vaccine series as of the end of March 2023, while primary series coverage was even lower in the state of Georgia, at 57%.[2] Uptake rates were initially high but began decreasing in the later months of 2021, have been consistently lower in younger age groups, and have tapered off markedly for subsequent doses.[2] Qualitative research indicates that this is due at least in part to vaccine hesitancy – a complex phenomenon related to concerns about the safety, efficacy, and necessity of these vaccines – which remains a considerable public health challenge.[3,4]

Encouraging higher vaccine uptake and allaying fears about vaccination are crucial to pandemic control. But the effects of vaccine promotion interventions can be difficult to predict, as individuals' decisions on whether to receive each vaccine dose and when to receive them are influenced by a multitude of factors. Dynamic transmission models, due to their ability to compare counterfactual scenarios and represent complex individual- and community-level behaviours, could provide insight into the optimal formulation and timing of such interventions. But while there exists a vast literature on mathematical models of vaccination decision-making, most of these models consider one-time decisions; are more focused on theory than on representing specific real-world scenarios; and, most crucially, are rooted in game theory, meaning they rely on the assumption of rational actors.[5-8] In contrast, social psychology suggests that individuals depend on heuristics rather than rational cost-benefit analyses when making complex decisions and that such decisions generally obey the law of inertia: they tend to remain stable over time but are sensitive to small "nudges" from unfavourable outcomes.[9,10]

In accordance with these findings, Papst et al developed an annual influenza model in which infections and vaccine costs (i.e., side effects) from past years could "nudge" persons to change their approach to vaccines.[11] This model, while theoretical in its focus, is consistent with the empirical findings of Walsh et al's longitudinal cohort study on trends in influenza vaccinations – specifically, that (1) in a given year, respondents were highly likely to repeat the decision they had made in the previous year, (2) respondents who changed their behaviour once were more likely to persist in their new behaviour than to switch back, and (3) those who forwent the vaccine but still became infected were more likely to switch to vaccinating in the future, while those who did receive the vaccine but still succumbed to infection were less likely to vaccinate again.[12] Thus, the role of heuristics and inertia in decision-making has been studied in the context of annual influenza vaccinations but is not yet well understood in the context of the ongoing COVID-19 vaccine rollout – which is analogous in that it is currently possible for people to receive up to five COVID-19 vaccine doses over time (with more possibly forthcoming), but distinct in that the ongoing COVID-19 pandemic lacks the predictable seasonality of the flu. Adapting the modelling techniques developed by Papst et al for integration into a dynamic mathematical model of SARS-CoV-2 transmission could provide insight into how vaccine promotion interventions should be formulated and targeted specifically to boost the stagnant levels of COVID-19 vaccine coverage in Georgia.

In this study, we utilized a network-based dynamic transmission model of SARS-CoV-2 coupled with a social-psychological decision-making model in which vaccine side effects, breakthrough infections, and the overall state of the outbreak could "nudge" individuals to change their attitudes towards vaccines. Our goal was to provide insight on how the overall epidemic outcomes might be impacted by interventions either on the probability that someone would cease to vaccinate after experiencing a breakthrough infection, or on the probability that someone would start to vaccinate after hospitalizations spiked in their community. We calibrated this model to reflect the local epidemic in the state of Georgia from January 2021 to August 2022 (i.e., from the month in which eligibility for the first vaccine dose began to expand in Georgia to the month before the start of the bivalent booster rollout) and aimed to make this work informative about the potential effects of interventions against vaccine hesitancy in the context of an ongoing pandemic.

## METHODS

In this study, we utilized a network-based model of SARS-CoV-2 transmission, disease progression, and vaccination behaviours in the population of Georgia, USA over a twenty-month period from the beginning of January 2021 to the end of August 2022. Our model was built and simulated using EpiModelCOVID, a previously validated extension of the EpiModel software platform.[13] This platform uses the statistical framework of exponential random graph models (ERGMs) to estimate and simulate a population's underlying contact patterns. For this study, we built a social-psychological decision-making model into EpiModelCOVID's existing vaccination module to explicitly simulate the dynamic vaccination decision-making process of each agent in the population. The model code and updated software are available on GitHub at https://github.com/EpiModel/COVID-Vax-Decisions and https://github.com/EpiModel/EpiModelCOVID/tree/Vax-Decisions, respectively.

### Core Model Structure

Our model tracked 100'000 individuals (agents), intended to represent the population of the state of Georgia, USA. Age was represented as a continuous attribute, with agents assigned an initial age (with one-year categories) at simulation start between 0 and 100 according to Georgia's age pyramid as of 2020.[14] Individuals could exit the model population at any time through death (general or disease-specific), with mortality rates varying by age. New individuals entered the model population exclusively through birth, with an assigned initial age of 0.

All modelled individuals were members of 2 distinct, overlapping contact network layers and transmission environments, representing the community and the home, respectively (**Figure 1**). For the community network layer, all contacts (edges) had a duration of one day – meaning each node could receive a new set of contacts at each daily time step, without regard for which nodes they were previously connected to. The overall cross-sectional mean degree across the population for this network layer was estimated at 13.8, based on the results of the COVIDVu study, which surveyed a probability sample of 3'112 U.S. households in spring 2021 and found 13.8 to be participants' mean number of daily contacts across all non-household settings (work, school, and other).[15] The mean degree for nodes aged 65 or older was specified to be less than the overall mean degree (specifically, 5.7), based on COVIDVu.[15] Additionally, based on the results of the POLYMOD social mixing study extrapolated to U.S. settings, age mixing assortativity was set at 69% for children (those under 18),

81% for adults (those aged at least 18 and under 65), and 21% for the elderly (those aged 65 and over).[16] The community environment was represented by an ERGM used to re-simulate contacts at each timestep in accordance with these network degree and age mixing targets.

In contrast to community edges, household edges were kept constant over time, lasting from simulation start or birth (whichever came first) to simulation end or death (whichever came first). For the household network layer, each agent was algorithmically assigned to a household according to six rules based on Census household composition data: (1) 29.2% of households had at least one member under 18,[17] (2) 79.1% of household had at least one member in the 18-to-64 age range,[17] (3) 31.4% of households had at least one member aged 65 or older,[17] (4) the average household had about 2.7 persons,[18] (5) every household with a child also had at least one adult, and (6) 97.9% of children had an adult under 65 in their household (**Figure 2**). Rule 6 was a simplifying assumption based on the Census finding that 2.1% of U.S. children lived with at least one grandparent and without a parent as of 2021.[19] This approach was taken to circumvent the lack of recent social mixing data for children in U.S. settings. Household edges were specified (without the use of an ERGM) such that each household was fully saturated and each edge was within a single household. Community and household contacts were subsequently combined to create a multi-layer dynamic network used in the final simulations.

Each model simulation was initialized with 865 persons in the exposed (infected but not infectious) state, in accordance with an estimate of the proportion of the Georgia population that was infected as of the start of July 2020.[20] Simulations were each run for an initial period of 180 daily time steps (corresponding to 5 July 2020 through 31 December 2020) for calibration purposes; the results of this calibration period were then used as the initial conditions for the simulation of our intervention timeframe of interest: a period of 608 days, corresponding to 1 January 2021 to 31 August 2022. Each scenario was simulated a total of 128 times.

Parameters defining the model's disease progression, transmission, and clinical epidemiology (**Table 1**) were either drawn from existing literature or calibrated as discussed below.

Our model represented the natural history of COVID-19 using a SEIRS framework (**Figure 3**). At simulation start, all individuals were either susceptible or exposed, and all new births entered the

population in the susceptible state. Once exposed via contact with an infectious person, newly infected individuals were stochastically assigned to either the asymptomatic or symptomatic clinical pathway, with the probability of symptoms dependent on age and vaccination status. Symptomatic individuals progressed from the exposed state through the infectious pre-symptomatic state to the infectious symptomatic state; from the infectious symptomatic state, individuals could stochastically enter the hospitalized state before recovery or directly enter the recovered state, with the probability of hospitalization also dependent on age and vaccination status. Asymptomatic individuals progressed directly from the exposed state to the asymptomatic state and then on to the recovered state. Once recovered, individuals stochastically re-entered the susceptible population, where they could be reinfected. Overall, individuals in the infectious pre-symptomatic, infectious symptomatic, or asymptomatic states were considered infectious, while individuals in the hospitalized state were subject to a higher age-specific mortality rate than those in other states to account for disease-related mortality.

This SEIRS framework allowed susceptible agents to stochastically transition from the susceptible to the exposed state (i.e., to become infected) upon contact with an infected person (i.e., a discordant contact). The per-day probability of infection given a discordant contact depended on the vaccination status of the susceptible agent, the symptom status of the infectious agent, and whether the contact was household-level or community-level. Asymptomatic infected persons had 50% the transmission potential of those with symptomatic infections.[21] Household contacts had about three times the per-day transmission potential of community contacts, accounting for increased opportunity for transmission via what were assumed to be closer, more sustained contacts. Interventions other than vaccination (such as case isolation) were not explicitly accounted for in the model, although their real-world effects were reflected in the calibrated transmission probabilities.

**Vaccination Decision-Making Process**

At simulation start or upon turning 18, whichever came first, each adult agent was assigned a binary "vaccinator type" attribute – resistant or willing – such that the prevalence of vaccine willingness by age group at the start of the vaccine rollout matched the empirical distribution measured in late 2020. The vaccination decision-making process for agents under age 18 was not explicitly modelled, since the vaccination decisions that parents/guardians make for their children are expected to be fundamentally different than the decisions they make for themselves; instead, the two youngest age

groups simply received vaccine doses according to age group-specific but otherwise homogenous rates.

In accordance with the law of inertia in decision-making,[9] agents maintained their initial attitude toward vaccination until an adverse event prompted them to reconsider. In the model, three such precipitating events were considered: (1) experiencing vaccine side effects could prompt a vaccine willing individual to become vaccine resistant, (2) experiencing an infection while fully vaccinated and (if applicable) up-to-date on booster doses (hereafter referred to as a "breakthrough infection") could prompt a vaccine willing individual to become vaccine resistant due to decreased trust in the vaccine, and (3) the hospitalized prevalence in the overall population crossing a certain threshold could prompt a vaccine resistant individual to become willing, due to heightened concern about the effects of the spread of COVID-19.

We identified (1) the odds ratio comparing the odds of booster willingness for those who had versus had not missed work due to side effects from the primary vaccination series[22] and (2) the odds ratio comparing the odds of booster willingness for those who had received the primary vaccination series and had versus had not been subsequently infected.[23] We then converted these odds ratios to risk differences so they could be interpreted as one-time probabilities of being "nudged" from vaccine willingness to vaccine resistance due to side effects or breakthrough infections, respectively. For the resistant-to-willing pathway, we estimated the probability that a vaccine-eligible adult in Georgia was convinced to vaccinate by an increase in hospitalized COVID-19 prevalence, by assuming that 38% of the late adopters who were vaccinated between July and September 2021 did so because of local hospitals filling with COVID-19 patients during that time, as the Delta variant spread.[24] Since the percentage of hospital beds in Georgia occupied by COVID-19 patients increased from about 2% to about 29% during this period,[25] we treated 20% as the threshold of interest; 20% of Georgia's 19'747 hospital beds translated to 3'895 hospitalized COVID patients out of Georgia's approximately 10.7 million people, or about 36 hospitalized COVID cases per 100'000 persons. Thus, hospitalized prevalence crossing 36 cases was treated as the precipitating event that could (potentially) convince vaccine resistant agents to become vaccine willing in our model.

**Vaccination Intervention**

The vaccination rollout in the model proceeded by age group (0 to 4, 5 to 17, 18 to 49, 50 to 64, and 65+), with the oldest group becoming eligible for the first dose on Day 11 of each simulation (corresponding to 11 January 2021, when everyone aged 65 or over became eligible for the first dose in Georgia).[26] Individuals became eligible for their second dose 21 days after receiving their first;[27] they became eligible for their first booster once (1) it had been rolled out to their age group and (2) six months had passed since they had received their second dose;[28] they then became eligible for their second booster once (1) it had been rolled out to their age group and (2) four months had passed since they received their first booster.[29] At any given timestep, individuals could stochastically undergo vaccination if (1) they were not currently symptomatic and had not tested positive in the last two weeks, (2) they were vaccine willing (for adult agents), and (3) they were currently eligible for their next dose based on their age group and vaccination history. Daily vaccination probabilities for those who fulfilled these criteria were age- and dose-specific and decayed over time to match the observed vaccination rates in Georgia.

Vaccination reduced the risk of disease acquisition, the risk of progression to symptomatic disease, and the risk of eventual hospitalization. These effects were dose specific. Vaccine immunity waned over time following an exponential decay pattern with a half-life of 80 days.[30]

**Calibration**

The per-act infection probability was manually calibrated so that the resultant number of incident infections by month matched the confirmed case counts reported by the Georgia Department of Public Health,[20] multiplied by five to account for underreporting[31] and scaled to a population of 100'000 (**Figure 4**). This per-act infection probability was allowed to vary over time by 30% of its reference value to account for time-dependent factors such as coverage of non-pharmaceutical interventions and the introduction of new variants. The daily act rate for the community network layer was assumed to be one (so that the per-act infection probability was equivalent to the daily infection probability for this layer); the daily act rate for the household network layer was calculated such that the total probability of infection from a household contact across a five-day infectious period approximately matched the secondary attack rate reported by a household transmission study.[32]

Similarly, the age-specific hospitalization proportions and disease-related mortality multiplier were calibrated so that the resultant hospital admissions and deaths by month matched the confirmed COVID-19 related hospitalizations and deaths reported by the Georgia Department of Public Health, scaled to a population of 100'000.[20]

Age- and dose-specific vaccination rates and the half-lives that controlled how quickly they decayed were manually calibrated so that the resultant vaccine coverage by age, dose, and month matched the levels reported by the CDC for Georgia (**Figure 5**).[2]

**Intervention Scenarios**

In addition to the reference scenario, in which vaccination coverage was calibrated to match reported levels, we modelled three sets of theoretical intervention scenarios. Within each set, we explored the impacts of (1) increasing the probability of a hospital capacity-related vaccine resistant-to-willing switch (hereafter referred to as the Hospitalization Nudge Probability or HNP) to as much as two times the reference value, and (2) decreasing the probability of a breakthrough infection-related vaccine willing-to-resistant switch (hereafter referred to as the Breakthrough Nudge Probability or BNP) to as little as zero. These changes were applied to all adults for our first set of scenarios, to older adults (those aged at least 65) only for our second set of scenarios, and to younger adults (those aged at least 18 and under 65) only for our third set of scenarios.

**Model Output**

For each model run, we tracked the cumulative number of incident SARS-CoV-2 infections, COVID hospitalizations, and COVID deaths, as well as the hospitalized prevalence over time. We also tracked the levels of vaccine willingness and per-dose vaccine coverage by age group over time. Our calculated summary metrics included cumulative incidence, cumulative deaths, number and percent of infections and deaths averted compared to the reference scenario, and infections and deaths averted per additional vaccine dose administered compared to the reference scenario. For each scenario, the median and 50% simulation interval of each metric across 128 simulations were reported.

## RESULTS

As seen in **Figure 4**, the simulated monthly incidence in the reference model closely matched the trends in the empirical, underreporting-adjusted monthly incidence in Georgia per 100'000 persons, with smaller peaks in January 2021 and September 2021, followed by a larger peak in January 2022 corresponding to the Omicron wave. The reference model's median number of infections across the January 2021 to August 2022 timeframe was 67'746.4 per 100'000 person-years (50% SI: (66'937.9, 68'534.7)), compared to the target of 45'824.3 infections per 100'000 person-years, while its median number of COVID-related deaths was 119.5 per 100'000 person-years (50% SI: (113.2, 124.0)), compared to the target of 128.6 deaths per 100'000 person-years.

In the reference model, the median number of vaccine doses administered (across all ages and doses) during the 20-month timeframe was 149'704.5 (50% SI: (149'471.2, 150'040.0)). **Figure 5** compares the trends over time in simulated vaccine coverage by age group and dose to the corresponding trends in empirical coverage. As shown in the first row of **Table 2**, the end cross-sectional coverage of the first dose was 71.5% (50% SI: (71.4%, 71.6%)) for 18- to 64-year-olds and 89.5% (50% SI: (89.3%, 89.7%)) for 65+ year-olds, compared to calibration targets of 73.3% and 92.4%, respectively. Final coverage of the second dose was 62.5% (50% SI: (62.3%, 62.6%)) for 18- to 64-year-olds and 81.1% (50% SI: (80.9%, 81.4%)) for 65+ year-olds, compared to targets of 61.2% and 81.2%, respectively. Final coverage of the third dose was 18.1% (50% SI: (18.0%, 18.2%)) for 18- to 49-year-olds, 34.3% (50% SI: (34.1%, 34.6%)) for 50- to 64-year-olds, and 51.8% (50% SI: (51.4%, 52.0%)) for 65+ year-olds, compared to targets of 17.5%, 34.5%, and 51.3%, respectively. Lastly, final coverage of the fourth dose was 7.4% (50% SI: (7.3%, 7.6%)) for 50- to 64-year-olds and 15.0% (50% SI: (14.9%, 15.3%)) for 65+ year-olds, compared to targets of 7.0% and 16.2%, respectively. These percentages represent coverage among the full population in each age group, not only the eligible population. Results for 18- to 49-year-olds and 50- to 64-year-olds were combined for the first two doses but treated separately for booster doses to match CDC vaccine coverage reports and because those under age 50 were not eligible for the fourth dose at all.

**Table 2** also shows the final vaccine coverage by age group and dose for a select set of intervention scenarios intended to be representative of the full range of scenarios tested. It shows that doubling the HNP for a particular age group generally led to a slight but noticeable increase in the coverage of

the first dose for that age group (for example, from a median of 71.5% to a median of 73.1% for 18- to 64-year-olds) but did not markedly impact coverage of subsequent doses. Meanwhile, reducing the BNP to zero for a particular age group generally led to a slight increase in coverage of the third and (if applicable) fourth dose for that age group (for example, from medians of 34.3% and 7.4% to medians of 35.0% and 7.7% for 50- to 64-year-olds, for the third and fourth doses respectively). Alongside **Table 2**, **Figure 6** shows how the total number of vaccine doses administered varied as the HNP varied from its reference value to twice its reference value and the BNP varied from its reference value to zero. The dose count generally increased as the HNP increased (i.e., as a vaccine resistant-to-willing switch was made more likely) and the BNP decreased (i.e., as a vaccine willing-to-resistant switch was made less likely), although the impact of the HNP was generally more pronounced, as indicated by the vertically skewed contours in **Figure 6**. Across all targeting approaches, the dose count was maximized when the HNP was maximized (i.e., doubled) and the BNP was minimized (i.e., reduced to zero). When all adults were targeted, the maximum number of doses administered across scenarios was 151'336.5 (50% SI: (151'063.0, 151'559.0)), for an excess of 1'632.0 doses (50% SI: (1'358.5, 1'854.5)) compared to the reference scenario; when only adults 65 years of age or older were targeted, the maximum number of doses across scenarios was 150'025.5 (50% SI: (149'804.8, 150,387.0)), for an excess of 321 doses (50% SI: (100.3, 682.5)); and when only adults under 65 were targeted, the maximum number of doses across scenarios was 151'096.0 (50% SI: (150'878.0, 151'372.3)), for an excess of 1'391.5 doses (50% SI: (1'173.5, 1'667.8)).

Analogously, **Table 3** and **Figure 7** show how varying the HNP and BNP affected cumulative incidence. The variation in the median cumulative incidence across scenarios was small compared to the variation in cumulative incidence across simulations within a single scenario, but **Figure 7** does indicate that slightly lower cumulative incidence results were more common when a high HNP was combined with a low BNP. When all adults were targeted, the minimum number of infections across scenarios was 67'111.7 per 100'000 person-years (50% SI: (66'344.0, 67'976.6)), corresponding to 634.7 (50% SI: (-230.2, 1'402.4)) infections averted per 100'000 person-years; this occurred when the HNP was doubled and the BNP was reduced to 60% of its reference value. When only older adults were targeted, the minimum number of infections across scenarios was 67'116.8 per 100'000 person-years (50% SI: (66'350.1, 68'493.4)), corresponding to 629.6 (50% SI: (-747.0, 1'396.3)) infections averted per 100'000 person-years; this occurred when the HNP was at 140% of its reference value and the BNP was at 0. When only younger adults were targeted, the minimum number of infections across

scenarios was 66'894.0 per 100'000 person-years (50% SI: (66'079.2, 67'932.5)), corresponding to 852.4 (50% SI: (-186.1, 1'667.2)) infections averted; this occurred when the HNP and BNP were at 180% and 10% of their reference values, respectively.

As shown in **Table 4** and **Figure 8**, the interventions had little to no impact on deaths, which did not vary according to any discernible systematic pattern across scenarios. When all adults were targeted, the minimum number of deaths across scenarios was 115.9 per 100'000 person-years (50% SI: (111.4, 122.8)), corresponding to 3.6 deaths averted per 100'000 person-years (50% SI: (-3.3, 8.1)) compared to the reference scenario; this occurred when the HNP and BNP were at 190% and 60% of their reference values, respectively. When only older adults were targeted, the minimum number of deaths across scenarios was 116.8 per 100'000 person-years (50% SI: (112.0, 123.4)), corresponding to 2.7 deaths averted per 100'000 person-years (50% SI: (-3.9, 7.5)); this occurred when the HNP and BNP were at 190% and 50% of their reference values, respectively. When only younger adults were targeted, the minimum number of deaths across scenarios was 116.2 per 100'000 person-years (50% SI: (111.2, 123.5)), corresponding to 3.3 deaths averted per 100'000 person-years (50% SI: (-4.0, 8.3)); this occurred when the HNP was doubled and the BNP was reduced to 40% of its reference value.

**Figure 9** shows the timing of the impact of the modelled interventions on vaccine coverage relative to the epidemic curve for five example scenarios. It shows that the epidemic curve was virtually indistinguishable across scenarios, while boosting the HNP caused a marked increase in the number of additional first doses delivered relative to the reference scenario, starting when the hospitalization threshold was typically crossed in mid-January 2022 and continuing until the end of the timeframe. However, these effects did not trickle down to subsequent doses, as also seen in **Table 2**. Suppressing the BNP caused a marked increase in the number of additional third and fourth doses delivered relative to the reference scenario; the additional third dose coverage built up throughout early 2022 (when the number of infections – and by extension, the number of breakthrough infections – was high) and plateaued when the number of infections decreased throughout spring 2022.

## DISCUSSION

In our study, we used a network-based mathematical model of SARS-CoV-2 transmission and vaccination decision-making to explore how manipulating the probabilities of changes in vaccine attitudes might impact vaccine coverage, disease incidence, and disease-related deaths. We found that while the theoretical interventions we modelled increased vaccine coverage, the additional vaccine-induced immunity built up too slowly compared to the rapid transmission of SARS-CoV-2 to markedly change the overall cumulative infections and deaths during our timeframe of interest. Essentially, in our stochastic model, the signal of the intervention effects was negligible compared to the noise of the random variations in incidence and deaths across model runs. We also found that increasing the probability that a spike in hospitalized prevalence would prompt vaccine hesitant persons to vaccinate (i.e., making resistant-to-willing switches more likely) generally had more of an impact on vaccination rates than decreasing the probability that breakthrough infections would prompt a previously vaccine willing person to forgo further vaccination (i.e., making willing-to-resistant switches less likely). These findings indicate that optimizing the timing of any vaccine promotion intervention relative to the timing of infection waves – so that the interventions anticipate the case curve instead of reacting to it – is crucial. They also highlight the importance of addressing baseline vaccine unwillingness to reduce the proportion of the population that is entirely vaccine-naïve.

The muted impact of our interventions on the final outcomes of cumulative incidence and deaths is likely due, at least in part, to the intervention effects' suboptimal timing. The modelled interventions acted slowly compared to the rapid transmission of SARS-CoV-2: for example, the hospitalized prevalence in our model generally crossed its threshold for the first time in January 2022, by which point most infections had already accrued, so the hospitalization nudge probability could only affect vaccine coverage during the last eight months of the modelled timeframe – when incidence was generally low to begin with and the number of infections that could potentially be averted was relatively small. If the model were run over a longer timeframe, allowing the intervention effects to build up over time, a long-term impact on incidence might become apparent, but the waves of infection during our twenty-month timeframe of interest were clearly unaffected in our model. Our findings diverge here from those of Papst et al and a preceding study by Wells et al, who implicitly assumed that each year's influenza vaccine rollout concluded before that year's outbreak began, and who found that under certain assumptions, infection waves could be eradicated biennially.[11,33] Our

results are, however, conceptually consistent with those of other COVID-19 modelling studies that have found the success of a particular vaccination campaign to be highly sensitive to its timing – for example, Gavish et al projected that advancing Israel's summer 2021 booster campaign by 2 weeks could have halved the number of cases in the subsequent three months.[34] The interventions we modelled were, by nature, reactive, in that they affected agents' responses to naturally occurring transmission events, but our findings indicate that proactive interventions – ones that anticipate transmission events like increases in hospitalized prevalence instead of capitalizing on them once they do occur – could have a more pronounced impact on epidemic outcomes.

Unlike our final outcomes of cumulative incidence and deaths, our intermediate outcome of vaccine doses administered was sensitive to the parameter changes that we tested, with the hospitalization nudge probability having more of an impact than the breakthrough nudge probability. In part, the relative importance of the hospitalization nudge probability follows from the "law of inertia" process that underlies our model: if someone was unvaccinated and vaccine-resistant, and an intervention prompted them to become vaccine-willing, they would tend to stay willing over time, and could receive up to four vaccine doses they would not have received otherwise. In contrast, if a vaccine willing person had received the primary vaccine sequence, and an intervention prompted them to stay vaccine willing, then they could receive at most two doses that they would not have received otherwise. The timing of the intervention effects relative to the vaccine rollout may also have contributed to the relatively higher impact of interventions on the hospitalization nudge probability: agents in our model were generally already eligible for the first two vaccine doses by the time such an intervention prompted them to make a resistant-to-willing switch they otherwise would not have made, meaning that they could act on their new vaccine views immediately. Meanwhile, agents who remained vaccine willing due to an intervention on the breakthrough nudge probability often did so well before they became eligible for subsequent doses, which occurred late in the model timeframe if it did at all.

Finally, we also found that limiting our intervention to older adults rather than targeting younger adults or all adults led to less of an impact on our outcomes. This is likely due in part to the relatively small size of the older age group and to their higher reference levels of vaccine willingness, which left less room for intervention-prompted increases. In conjunction with previous modelling studies that have illustrated the benefits of vaccinating younger age groups that are less susceptible to severe disease or death but play a larger role in transmission,[34-36] our study highlights the importance of broadly

addressing vaccine hesitancy in younger populations for whom COVID-19 vaccine willingness was lower to begin with.

*Limitations.* One of the major limitations of our model is our simplified representation of the vaccination decision-making process. We only considered three factors that could affect an individual's decisions: their own experience of vaccine side-effects, their own experience of breakthrough infections, and overall hospitalized prevalence. There may be many others, including (but not limited to) employer mandates,[24] social conformity,[24,37] friends' and family members' experiences with vaccines and COVID-19,[24,38] and the spread of information via news outlets and social media.[39] Of the three factors we considered, only one (side effects) could cause people to become vaccine resistant after their first dose (before they were considered fully vaccinated and therefore able to experience a breakthrough infection), and this relatively minor pathway could not fully account for the significant number of people in Georgia who received their first dose but not their second. Instead, our model manufactured this drop-off through manipulation of the vaccination rates: our calibration resulted in initially high rates for the second dose that decayed very quickly, to replicate the real-life dichotomy between persons who received their second dose promptly after the recommended interval and persons who never received it at all. Since the vaccination rates were kept constant across scenarios, these parameters muted the impact of our interventions on the resistant-to-willing pathway: because the daily probability of receiving the second dose among the vaccine willing decayed so quickly over time, an unreasonably high number of the newly willing agents nudged by the spike in hospitalizations ended up getting the first dose but not the second and therefore never moved past partial vaccine-induced immunity. Future work on this model should explore different ways of realizing the drop-off between the first two doses that do not exaggerate this effect for late adopters of the vaccine.

A further limitation of our model is the considerable uncertainty to which some of our parameters are subject. Since COVID-19 emerged relatively recently, data on the duration of vaccine-induced and natural immunity is currently limited. We represented waning vaccine immunity using an exponential decay process based off the half-life of post-vaccination serum antibody levels and waning natural immunity using an all-or-nothing approach (with a period of on average 270 days in which recovered agents were completely protected from infection, followed by a return to pre-infection levels of susceptibility). Both methodologies are potentially flawed, especially as they do not account for heterogeneities in immunity duration by age, disease severity, or other factors.[40-42] We also arrived at

our reference willing-to-resistant nudge probabilities by extrapolating data from surveys of vaccine willingness beyond their intended use. In the future, sensitivity analyses should be performed on these particularly uncertain parameters.

## CONCLUSIONS

Our results show how dynamical transmission models that are calibrated to empirical data and that include realistic details of human behaviour, based on established results in social psychology, can generate predictions that diverge from the results of simpler models that, for example, assume homogenized behaviour patterns or are not validated against appropriate data. This illustrates how models with greater psychological realism can be useful for informing public health interventions. Specifically, our findings indicate that reactive vaccination interventions may have only a limited ability to avert infection waves in the short-term, suggesting that attention should be paid to formulating vaccine promotion interventions that accurately anticipate the case curve instead of reacting to it.

## TABLES AND FIGURES

### Table 1. Model parameters

| Parameter | Value | Source |
|---|---|---|
| **Population Characteristics** | | |
| *Total population size* | 100'000 | Assumed |
| *Proportion of population aged under 18* | 0.233 | http://wonder.cdc.gov/bridged-race-v2020.html [14] |
| *Proportion of population aged at least 18 and under 65* | 0.620 | http://wonder.cdc.gov/bridged-race-v2020.html [14] |
| *Proportion of population aged over 65* | 0.147 | http://wonder.cdc.gov/bridged-race-v2020.html [14] |
| **Household Characteristics** | | |
| *Average household size* | 2.7 | https://www.census.gov/quickfacts/ [18] |
| *Proportion of households with a member aged under 18* | 0.292 | Census Table H2 2020 [17] |
| *Proportions of households with a member aged at least 18 and under 65* | 0.791 | Census Table H2 2020 [17] |
| *Proportion of households with a member aged at least 65* | 0.314 | Census Table H2 2020 [17] |
| *Proportion of children living with a person aged 18 or older* | 1.0 | Assumed |
| *Proportion of children living with a person aged at least 18 and under 65* | 0.979 | Census Table C4 2021 [19] |
| **Community Contact Patterns** | | |
| *Overall daily mean degree* | 13.8 | Nelson et al 2022 [15] |
| *Daily mean degree for persons aged 65 and over* | 5.7 | Nelson et al 2022 [15] |
| *Associative mixing proportion for persons aged under 18* | 0.69 | Prem et al 2017 [16] |
| *Associative mixing proportion for persons aged at least 18 and under 65* | 0.81 | Prem et al 2017 [16] |
| *Associative mixing proportion for persons aged at least 65* | 0.21 | Prem et al 2017 [16] |
| **Transmission** | | |
| *Reference per-act transmission probability* | 0.050 | Calibrated |
| *Per-act transmission probability during periods of decreased transmission* | 0.035 | Calibrated |

| | | |
|---|---|---|
| *Per-act transmission probability during periods of increased transmission* | 0.065 | Calibrated |
| *Relative risk of transmission for asymptomatic individuals* | 0.5 | Davies et al 2020 [21] |
| *Contacts per pairing per day for community-level pairings* | 1 | Assumed |
| *Contacts per pairing per day for household-level pairings* | 3 | Calculated from Madewell et al 2022 [32] |
| **Natural History** | | |
| *Proportion symptomatic, per decade of age* | 0.573, 0.642, 0.760, 0.800, 0.813, 0.814, 0.769, 0.723, 0.666 | Harrington 2022 [43] |
| *Proportion hospitalized given symptomatic infection, per decade of age* | 0.006, 0.006, 0.008, 0.015, 0.021, 0.027, 0.036, 0.046, 0.054 | Calibrated, with ratios from Harrington 2022 [43] |
| *Average duration of latent period, in days* | 5.5 | Xin et al 2022 [44] |
| *Average duration of pre-clinical infectious period, in days* | 1.5 | Davies et al 2020 [21] |
| *Average duration of clinical infectious period prior to hospitalization, in days* | 3.0 | Harrington 2022 [43] |
| *Average duration of clinical infectious period prior to recovery, in days* | 3.5 | Davies et al 2020 [21] |
| *Average duration of hospitalization, in days* | 10.0 | Conlon et al 2021 [45] |
| *Average duration of asymptomatic infectious period, in days* | 5.0 | Davies et al 2020 [21] |
| *Average duration of immunity after recovery, in days* | 270 | https://www.cdc.gov/coronavirus/2019-ncov/science/science-briefs/vaccine-induced-immunity.html [30] |
| *Birth rate, in births per 100'000 persons per year* | 1399 | Assumed (to maintain stable population size) |
| *General annual mortality rate, in deaths per 100'000 persons per year** | 608, 30, 13, 22, 63, 116, 143, 187, 228, 300, 416, 600, 945, 1453, 1952, 2817, 4369, 7159, 15626 | https://oasis.state.ga.us/oasis/WebQuery/qryMortality.aspx [46] |
| *COVID-related mortality multiplier* | 1800 | Calibrated |
| **Testing** | | |
| *Testing rate for symptomatic persons* | 0.10 | Jenness et al 2021 [47] |
| *General testing rate* | 0.01 | Jenness et al 2021 [47] |
| *PCR test sensitivity* | 0.80 | Lopman et al 2021 [48] |
| **Vaccination Decision-Making** | | |

| | | |
|---|---|---|
| *Proportion initially vaccine willing* | | |
| *Ages 18 - 49* | 0.70 | Kelly et al 2021 [49] |
| *Ages 50 - 64* | 0.75 | Kelly et al 2021 [49] |
| *Ages 65+* | 0.91 | Nikolovski et al 2021 [50] |
| *Probability of resistant-to-willing switch due to hospitals approaching capacity* | 0.102 | Calculated from Hamel et al 2021 [24] |
| *Probability of willing-to-resistant switch due to vaccine side effects* | 0.073 | Chrissian et al 2022 [22] |
| *Probability of willing-to-resistant switch due to breakthrough infection* | 0.125 | Dziedzic et al 2022 [23] |
| *Hospitalization threshold, in cases per 100'000 persons* | 36 | covid.cdc.gov/covid-data-tracker/#hospital-capacity [25] |
| **Vaccination** | | |
| *Time step for start of dose 1 rollout (in parentheses: corresponding calendar date)* | | |
| *Ages 0 to 4* | Day 534 (18 Jun. 2022) | https://www.cdc.gov/media/releases/2022/s0618-children-vaccine.html [51] |
| *Ages 5 to 17* | Day 132 (12 May 2021) | www.nytimes.com/2021/05/12/health/coronavirus-vaccine-children.html [52] |
| *Ages 18 to 49* | Day 84 (25 Mar. 2021) | https://www.ajc.com/politics/S2TLG4G3CBDNJBUPPRROV5ROSI/ [53] |
| *Ages 50 to 64* | Day 74 (15 Mar. 2021) | https://www.ajc.com/politics/PO4VMZ3Q3NA25LPQB6CNDW7PAA/ [54] |
| *Ages 65+* | Day 11 (11 Jan. 2021) | https://publichealthathens.com/ [26] |
| *Time step for start of dose 3 rollout (in parentheses: corresponding calendar date)* | | |
| *Ages 5 to 17* | Day 368 (3 Jan. 2022) | https://www.fda.gov/news-events/press-announcements/ [55] |
| *Ages 18 to 49* | Day 323 (19 Nov. 2021) | https://www.cdc.gov/media/releases/2021/s1119-booster-shots.html [56] |
| *Ages 50 to 64* | Day 323 (19 Nov. 2021) | https://www.cdc.gov/media/releases/2021/s1119-booster-shots.html [56] |
| *Ages 65+* | Day 265 (22 Sep. 2021) | https://www.fda.gov/news-events/press-announcements/ [28] |
| *Time step for start of dose 4 rollout (in parentheses: corresponding calendar date)* | | |
| *Ages 50 to 64* | Day 453 (29 Mar. 2022) | https://www.fda.gov/news-events/press-announcements/ [29] |
| *Ages 65+* | Day 453 (29 Mar. 2022) | https://www.fda.gov/news-events/press-announcements/ [29] |

| | | |
|---|---|---|
| *Dose 1 vaccination rate, per day (in parentheses: rate half-life, in days)* | | |
| *Ages 0 to 4* | 0.0005 (365) | Calibrated |
| *Ages 5 to 17* | 0.0020 (220) | Calibrated |
| *Ages 18 to 49* | 0.0210 (160) | Calibrated |
| *Ages 50 to 64* | 0.0210 (160) | Calibrated |
| *Ages 65+* | 0.0200 (365) | Calibrated |
| *Dose 2 vaccination rate, per day (in parentheses: rate half-life, in days)* | | |
| *Ages 0 to 4* | 0.0100 (365) | Calibrated |
| *Ages 5 to 17* | 0.5400 (60) | Calibrated |
| *Ages 18 to 49* | 0.6500 (30) | Calibrated |
| *Ages 50 to 64* | 0.6500 (30) | Calibrated |
| *Ages 65+* | 0.2500 (40) | Calibrated |
| *Dose 3 vaccination rate, per day (in parentheses: rate half-life, in days)* | | |
| *Ages 5 to 17* | 0.0050 (60) | Calibrated |
| *Ages 18 to 49* | 0.0100 (35) | Calibrated |
| *Ages 50 to 64* | 0.0250 (30) | Calibrated |
| *Ages 65+* | 0.0200 (50) | Calibrated |
| *Dose 4 vaccination rate, per day (in parentheses: rate half-life, in days)* | | |
| *Ages 50 to 64* | 0.0050 (60) | Calibrated |
| *Ages 65+* | 0.0050 (80) | Calibrated |
| *Minimum interval between doses 1 and 2, in days* | 21 | https://www.cdc.gov/vaccines/covid-19/info-by-product/index.html [27] |
| *Minimum interval between doses 2 and 3, in days* | 180 | https://www.fda.gov/news-events/press-announcements/ [28] |
| *Minimum interval between doses 3 and 4, in days* | 120 | https://www.fda.gov/news-events/press-announcements/ [29] |
| *Relative risk of infection at peak of vaccine immunity* | | |

| | | |
|---|---|---|
| *Dose 1* | 0.324 | Pilishvili et al 2021 [57] |
| *Dose 2* | 0.112 | Pilishvili et al 2021 [57] |
| *Dose 3* | 0.120 | Barda et al 2021 [58] |
| *Dose 4* | 0.120 | Barda et al 2021 [58] |
| *Relative risk of symptomatic disease at peak of vaccine immunity* | | |
| *Dose 1* | 0.400 | Chung et al 2021 [59] |
| *Dose 2* | 0.090 | Chung et al 2021 [59] |
| *Dose 3* | 0.090 | Barda et al 2021 [58] |
| *Dose 4* | 0.090 | Barda et al 2021 [58] |
| *Relative risk of hospitalization at peak of vaccine immunity* | | |
| *Dose 1* | 0.300 | Chung et al 2021 [59] |
| *Dose 2* | 0.020 | Chung et al 2021 [59] |
| *Dose 3* | 0.070 | Barda et al 2021 [58] |
| *Dose 4* | 0.070 | Barda et al 2021 [58] |
| *Per-dose probability of vaccine side effects* | 0.180 | Chrissian et al 2022 [22] |
| *Half-life of vaccine immunity, in days* | 80 | https://www.cdc.gov/coronavirus/2019-ncov/science/science-briefs/vaccine-induced-immunity.html [30] |

* Rates displayed for the following age groups: <1, 1-4, 5-9, 10-14, 15-19, 20-24, 25-29, 30-34, 35-39, 40-44, 45-49, 50-54, 55-59, 60-64, 65-69, 70-74, 75-79, 80-84, 85+

**Table 2. Proportion of adult population vaccinated, by dose and age group, for select scenarios.** Green indicates higher coverage than the reference level. Corresponding 50% simulation intervals are shown in the appendix in Table A1.

| Scenario | | | Ages 18 - 49 | | | Ages 50 - 64 | | | |
|---|---|---|---|---|---|---|---|---|---|
| Targeting | Hospitalization Nudge Prob. | Breakthrough Nudge Prob. | Dose 1 % | Dose 2 % | Dose 3 % | Dose 1 % | Dose 2 % | Dose 3 % | Dose 4 % |
| - | Reference | Reference | 71.5 | 62.5 | 18.1 | 71.5 | 62.5 | 34.3 | 7.4 |
| All Adults (18+) | 200% of Reference | Reference | 73.1 | 62.5 | 18.1 | 73.1 | 62.5 | 34.3 | 7.4 |
| | Reference | 50% of Reference | 71.5 | 62.5 | 18.3 | 71.5 | 62.5 | 34.6 | 7.5 |
| | Reference | 0% of Reference | 71.5 | 62.5 | 18.4 | 71.5 | 62.5 | 35.0 | 7.7 |
| | 200% of Reference | 50% of Reference | 73.0 | 62.5 | 18.3 | 73.0 | 62.5 | 34.7 | 7.6 |
| | 200% of Reference | 0% of Reference | 73.1 | 62.5 | 18.4 | 73.1 | 62.5 | 35.0 | 7.7 |
| Older Adults (65+) | 200% of Reference | Reference | 71.5 | 62.5 | 18.1 | 71.5 | 62.5 | 34.3 | 7.4 |
| | Reference | 50% of Reference | 71.5 | 62.6 | 18.1 | 71.5 | 62.6 | 34.3 | 7.4 |
| | Reference | 0% of Reference | 71.5 | 62.5 | 18.1 | 71.5 | 62.5 | 34.3 | 7.4 |
| | 200% of Reference | 50% of Reference | 71.5 | 62.5 | 18.1 | 71.5 | 62.5 | 34.3 | 7.4 |
| | 200% of Reference | 0% of Reference | 71.5 | 62.5 | 18.1 | 71.5 | 62.5 | 34.4 | 7.4 |
| Younger Adults (18 - 64) | 200% of Reference | Reference | 73.1 | 62.5 | 18.1 | 73.1 | 62.5 | 34.3 | 7.5 |
| | Reference | 50% of Reference | 71.5 | 62.5 | 18.3 | 71.5 | 62.5 | 34.6 | 7.6 |
| | Reference | 0% of Reference | 71.5 | 62.5 | 18.4 | 71.5 | 62.5 | 35.0 | 7.7 |
| | 200% of Reference | 50% of Reference | 73.0 | 62.5 | 18.3 | 73.0 | 62.5 | 34.6 | 7.5 |
| | 200% of Reference | 0% of Reference | 73.1 | 62.5 | 18.5 | 73.1 | 62.5 | 35.0 | 7.7 |

| Scenario | | | Ages 65+ | | | |
|---|---|---|---|---|---|---|
| **Targeting** | **Hospitalization Nudge Probability** | **Breakthrough Nudge Probability** | Dose 1 % | Dose 2 % | Dose 3 % | Dose 4 % |
| - | Reference | Reference | 89.5 | 81.1 | 51.8 | 15.0 |
| All Adults (18+) | 200% of Reference | Reference | 90.5 | 81.2 | 51.9 | 15.1 |
| | Reference | 50% of Reference | 89.5 | 81.1 | 52.0 | 15.2 |
| | Reference | 0% of Reference | 89.6 | 81.1 | 52.3 | 15.4 |
| | 200% of Reference | 50% of Reference | 90.4 | 81.1 | 52.1 | 15.3 |
| | 200% of Reference | 0% of Reference | 90.5 | 81.1 | 52.2 | 15.3 |
| Older Adults (65+) | 200% of Reference | Reference | 90.4 | 81.2 | 51.8 | 15.1 |
| | Reference | 50% of Reference | 89.6 | 81.1 | 52.1 | 15.2 |
| | Reference | 0% of Reference | 89.5 | 81.1 | 52.1 | 15.3 |
| | 200% of Reference | 50% of Reference | 90.3 | 81.1 | 52.0 | 15.2 |
| | 200% of Reference | 0% of Reference | 90.4 | 81.1 | 52.2 | 15.4 |
| Younger Adults (18 - 64) | 200% of Reference | Reference | 89.6 | 81.1 | 51.8 | 15.0 |
| | Reference | 50% of Reference | 89.5 | 81.1 | 51.8 | 15.1 |
| | Reference | 0% of Reference | 89.6 | 81.2 | 51.8 | 15.0 |
| | 200% of Reference | 50% of Reference | 89.6 | 81.1 | 51.9 | 15.0 |
| | 200% of Reference | 0% of Reference | 89.6 | 81.1 | 51.8 | 15.0 |

**Table 3. Cumulative infections and infections averted by end of simulation, for select scenarios.** Green indicates fewer infections than the reference level and orange indicates more. Corresponding 50% simulation intervals are available in the appendix in Table A2.

| Scenario | | | Total Infections per 100'000 PY | Infections Averted per 100'000 PY | Percent of Infections Averted | Infections Averted per Addtl. Dose |
|---|---|---|---|---|---|---|
| **Targeting** | **Hospitalization Nudge Prob.** | **Breakthrough Nudge Prob.** | *n* | *n* | *%* | *n* |
| - | Reference | Reference | 67'746.4 | - | - | - |
| All Adults (18+) | 200% of Reference | Reference | 67'256.6 | 489.8 | 0.7 | 0.5 |
| | Reference | 50% of Reference | 67'701.8 | 44.6 | 0.1 | 0.1 |
| | Reference | 0% of Reference | 67'632.6 | 113.8 | 0.2 | 0.2 |
| | 200% of Reference | 50% of Reference | 67'531.7 | 214.7 | 0.3 | 0.2 |
| | 200% of Reference | 0% of Reference | 67'270.7 | 475.7 | 0.7 | 0.3 |
| Older Adults (65+) | 200% of Reference | Reference | 67'435.0 | 311.4 | 0.5 | 0.4 |
| | Reference | 50% of Reference | 67'542.2 | 204.2 | 0.3 | 0.4 |
| | Reference | 0% of Reference | 67'638.6 | 107.8 | 0.2 | 0.0 |
| | 200% of Reference | 50% of Reference | 67'786.2 | -39.8 | -0.1 | -0.2 |
| | 200% of Reference | 0% of Reference | 67'412.9 | 333.5 | 0.5 | 1.2 |
| Younger Adults (18 - 64) | 200% of Reference | Reference | 67'358.1 | 388.3 | 0.6 | 0.6 |
| | Reference | 50% of Reference | 67'702.4 | 44.0 | 0.1 | 0.3 |
| | Reference | 0% of Reference | 67'527.5 | 218.9 | 0.3 | 0.1 |
| | 200% of Reference | 50% of Reference | 67'182.0 | 564.4 | 0.8 | 0.5 |
| | 200% of Reference | 0% of Reference | 67'294.0 | 452.4 | 0.7 | 0.4 |

**Table 4. Cumulative deaths and deaths averted by end of simulation, for select scenarios.** Green indicates fewer deaths than the reference level and orange indicates more. Corresponding 50% simulation intervals are available in the appendix in Table A3.

| Scenario | | | Total Deaths per 100'000 PY | Deaths Averted per 100'000 PY | Percent of Deaths Averted | Deaths Averted per Addtl. Dose |
|---|---|---|---|---|---|---|
| **Targeting** | **Hospitalization Nudge Prob.** | **Breakthrough Nudge Prob.** | *n* | *n* | *%* | *n* |
| - | Reference | Reference | 119.5 | - | - | - |
| All Adults (18+) | 200% of Reference | Reference | 118.3 | 1.2 | 1.0 | 0.0 |
| | Reference | 50% of Reference | 118.6 | 0.9 | 0.8 | 0.0 |
| | Reference | 0% of Reference | 119.2 | 0.3 | 0.3 | 0.0 |
| | 200% of Reference | 50% of Reference | 117.1 | 2.4 | 2.0 | 0.0 |
| | 200% of Reference | 0% of Reference | 119.2 | 0.3 | 0.3 | 0.0 |
| Older Adults (65+) | 200% of Reference | Reference | 118.6 | 0.9 | 0.8 | 0.0 |
| | Reference | 50% of Reference | 117.1 | 2.4 | 2.0 | 0.0 |
| | Reference | 0% of Reference | 118.6 | 0.9 | 0.8 | 0.0 |
| | 200% of Reference | 50% of Reference | 118.3 | 1.2 | 1.0 | 0.0 |
| | 200% of Reference | 0% of Reference | 120.4 | -0.9 | -0.8 | 0.0 |
| Younger Adults (18 - 64) | 200% of Reference | Reference | 116.8 | 2.7 | 2.3 | 0.0 |
| | Reference | 50% of Reference | 120.7 | -1.2 | -1.0 | 0.0 |
| | Reference | 0% of Reference | 117.4 | 2.1 | 1.8 | 0.0 |
| | 200% of Reference | 50% of Reference | 118.9 | 0.6 | 0.5 | 0.0 |
| | 200% of Reference | 0% of Reference | 119.2 | 0.3 | 0.3 | 0.0 |

**Figure 1. Network schematic.** All agents in the model were part of two distinct contact network layers, representing the household and the community, respectively. The community network layer was intended to encompass all non-household contacts, including workplace, school, social, and other contacts. The household network layer was static, with agents assigned a household at simulation start or birth and remaining in contact with all other members of that household until simulation end or death. The community network layer, in contrast, reset each day, with the number and age distribution of daily contacts for each agent depending on that agent's age.

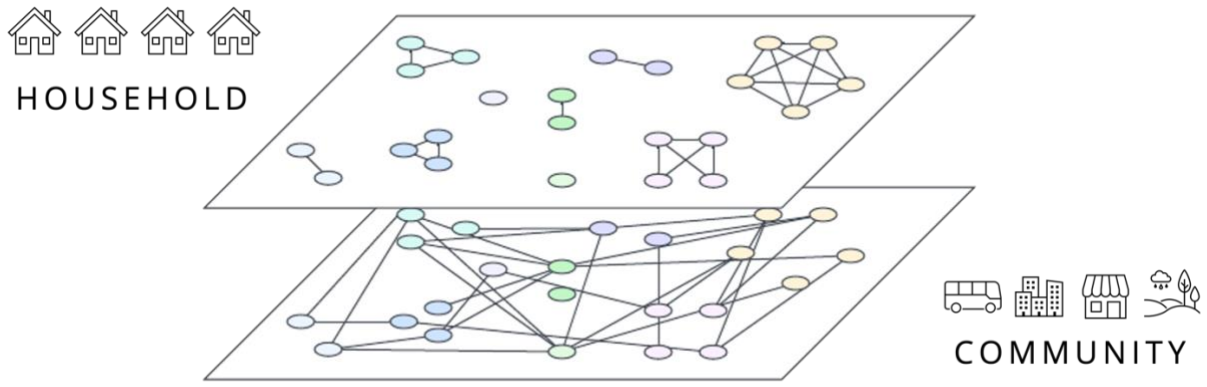


**Figure 2. Household assignment example.** This figure illustrates the household assignment algorithm with an example set of 100 agents, each assigned an age category ('C' for child, 'A' for adult, or 'E' for elderly) according to the age distribution of the Georgia population. These 100 agents are shown divided among 37 households (for an overall average household size of about 2.7), such that 29.2% of households have at least one child, 79.1% of household have at least one adult, 31.4% of households have at least one elderly person, every child lives with at least one adult or elderly person, and 97.9% of children live with at least one non-elderly adult. (Due to the small number of nodes in this example, the percentages do not work out exactly, as they do with the 100'000 nodes in the full model.)

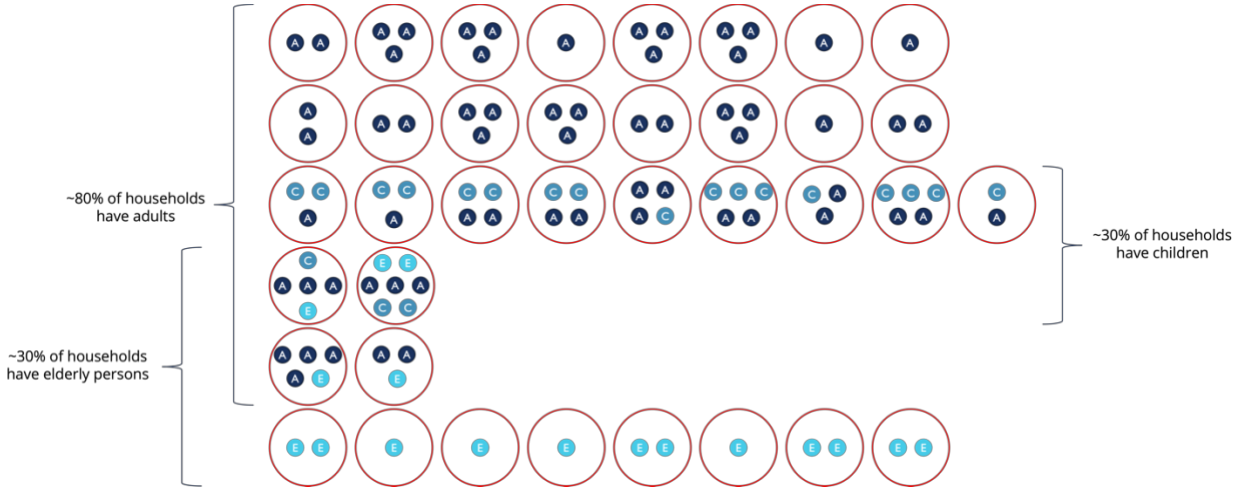


**Figure 3. Model flow diagram.** The model's SARS-CoV-2 transmission and COVID-19 disease progression processes were represented as stochastic transitions in the modified Susceptible-Exposed-Infected-Recovered compartmental framework shown below.

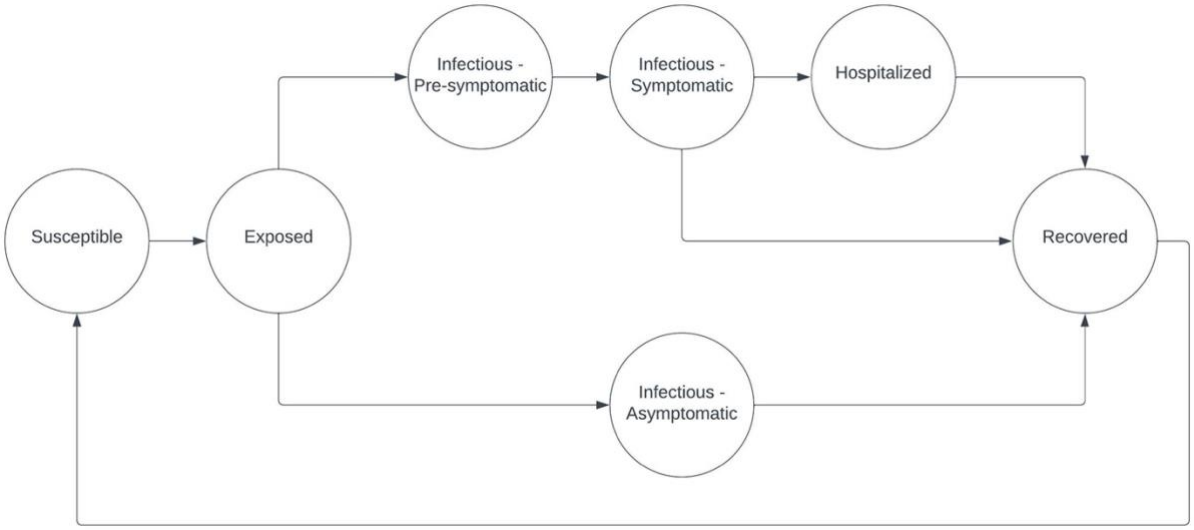


**Figure 4. Model calibration results for cases, hospitalizations, and deaths.** The reference model was calibrated to (1) an estimate of the total number of incident SARS-CoV-2 infections, (2) the reported number of confirmed COVID-19-related hospital admissions, and (3) the reported number of confirmed COVID-19-related deaths, all per 100'000 persons in Georgia per month.

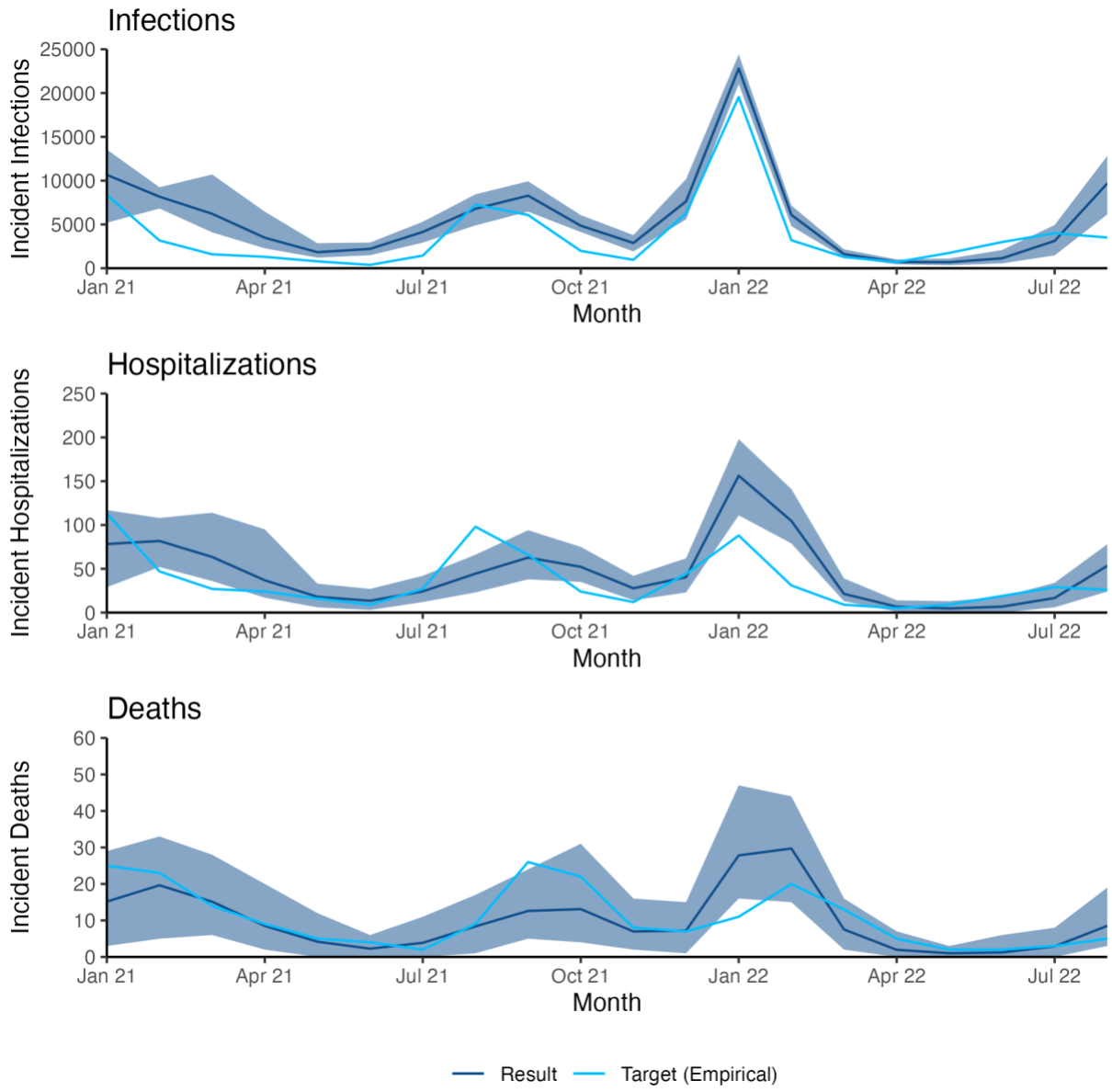


**Figure 5. Model calibration results for vaccine coverage.** The reference model was also calibrated to the reported vaccine coverage levels in Georgia by age group, dose, and month.

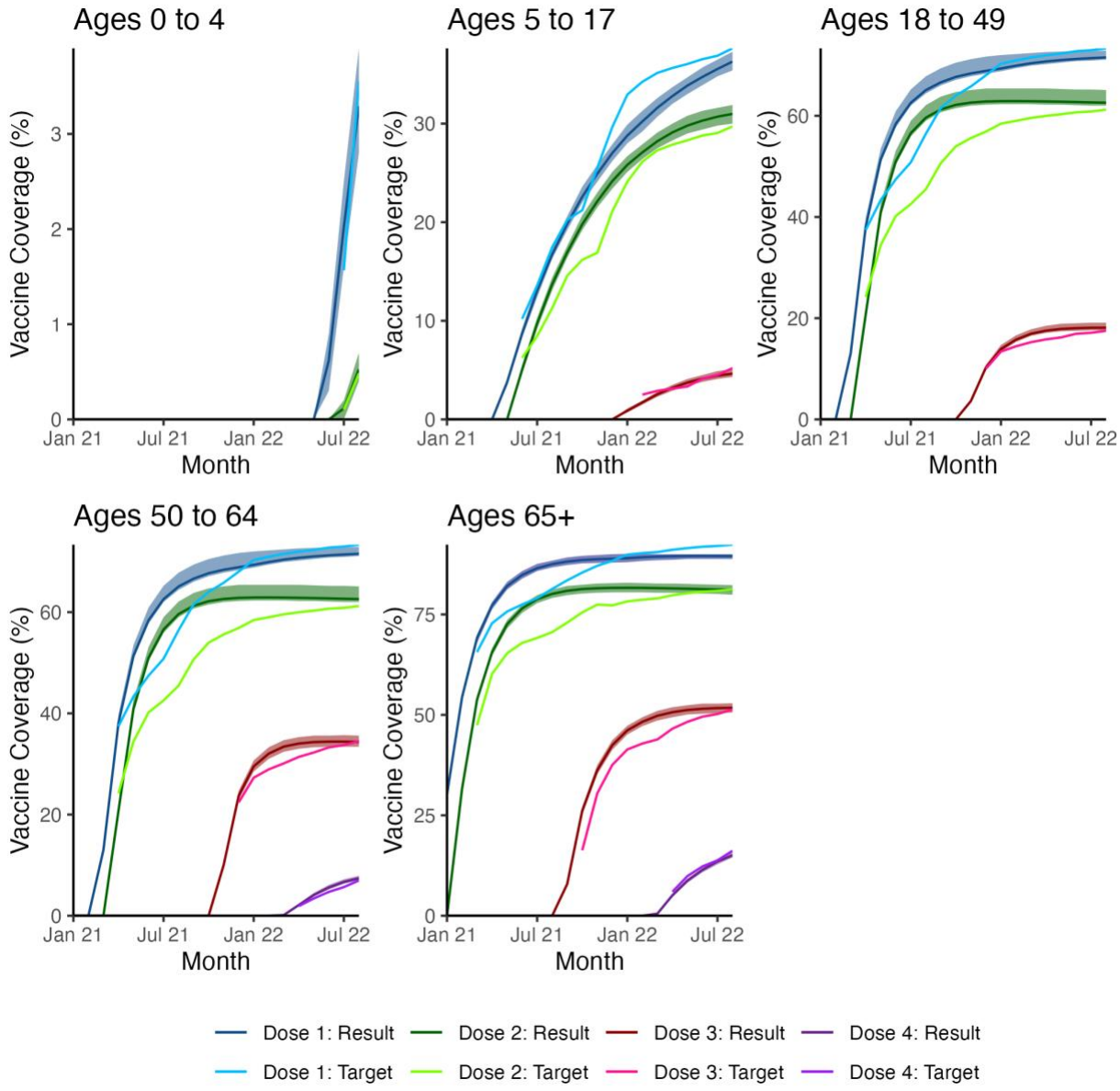


**Figure 6. Cumulative vaccine doses administered by end of simulation, by model scenario.** The hospitalization nudge probability (abbreviated as HNP) was increased from 100% to 200% of its reference value in increments of 10%; the breakthrough nudge probability (abbreviated as BNP) was decreased from 100% to 0% of its reference value in increments of 10%. For each parameter combination, the median number of doses administered per run across 128 runs is displayed.

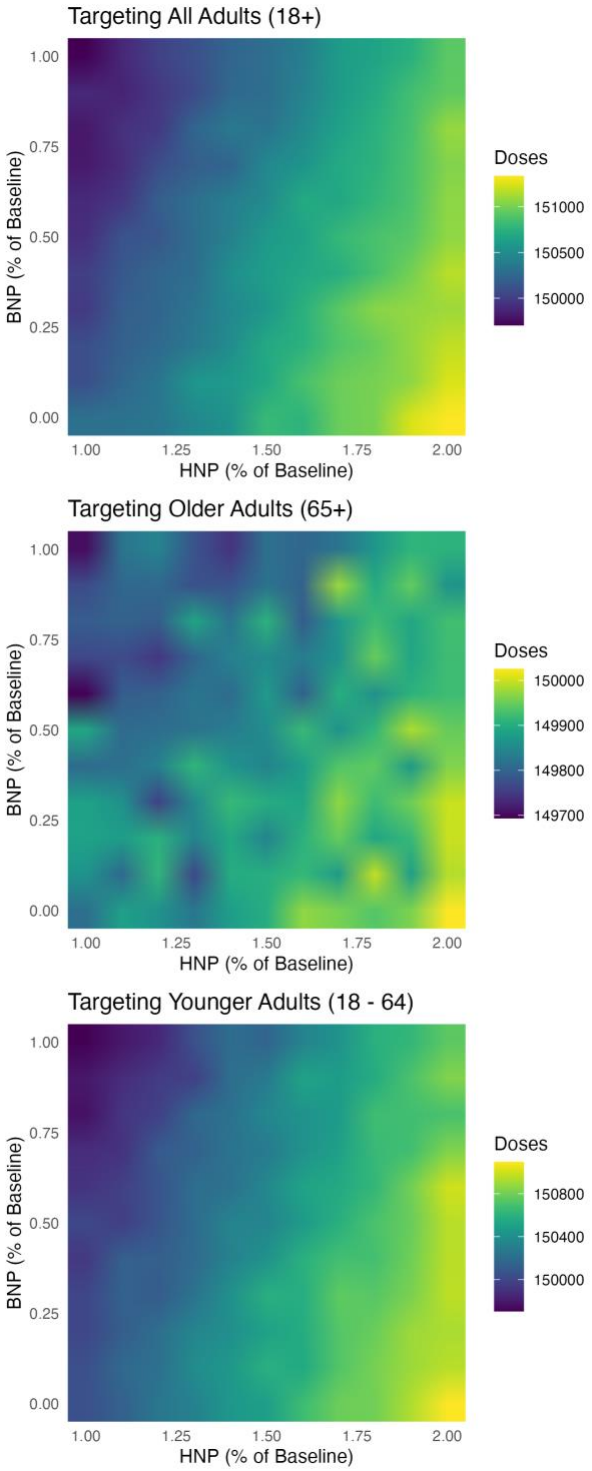


**Figure 7. Cumulative incidence per 100'000 PY, by model scenario.** The hospitalization nudge probability (abbreviated as HNP) was increased from 100% to 200% of its reference value in increments of 10%; the breakthrough nudge probability (abbreviated as BNP) was decreased from 100% to 0% of its reference value in increments of 10%. For each parameter combination, the median cumulative incidence (scaled to 100'000 person-years) across 128 simulations is displayed.

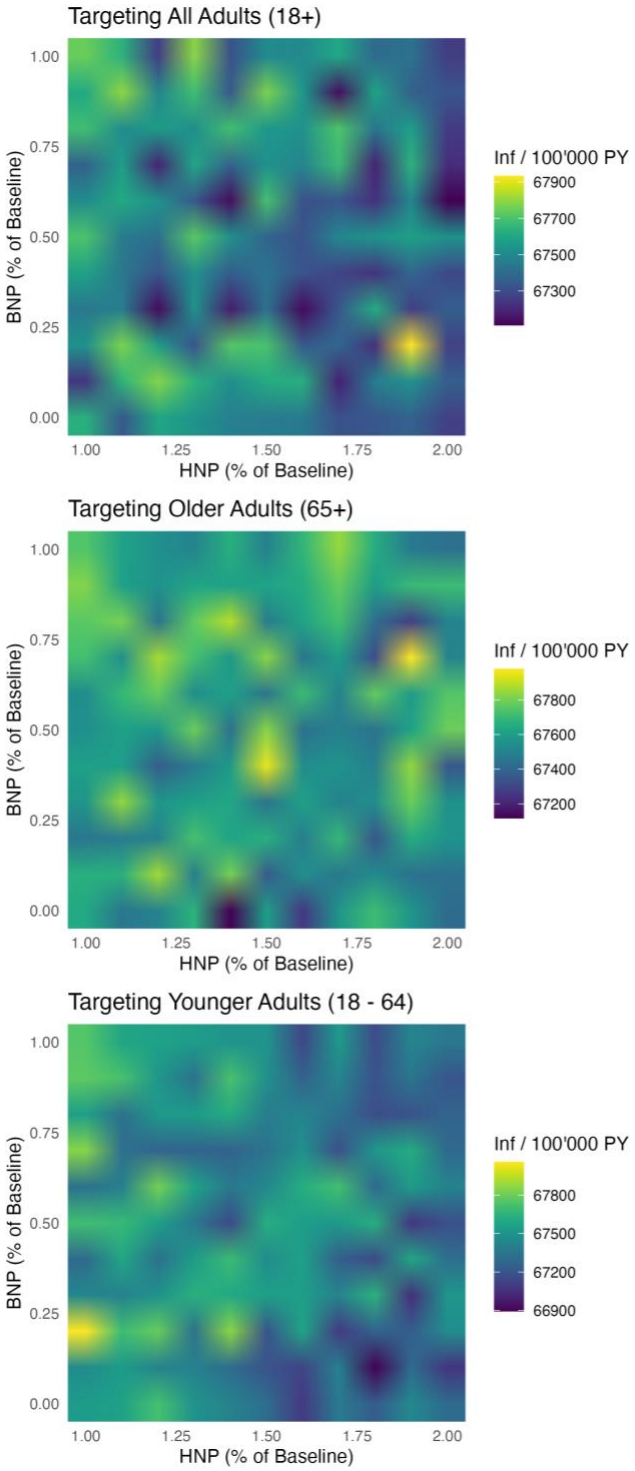


**Figure 8. Cumulative deaths per 100'000 PY, by model scenario.** The hospitalization nudge probability (abbreviated as HNP) was increased from 100% to 200% of its reference value in increments of 10%; the breakthrough nudge probability (abbreviated as BNP) was decreased from 100% to 0% of its reference value in increments of 10%. For each parameter combination, the median cumulative death count (scaled to 100'000 person-years) across 128 simulations is displayed.

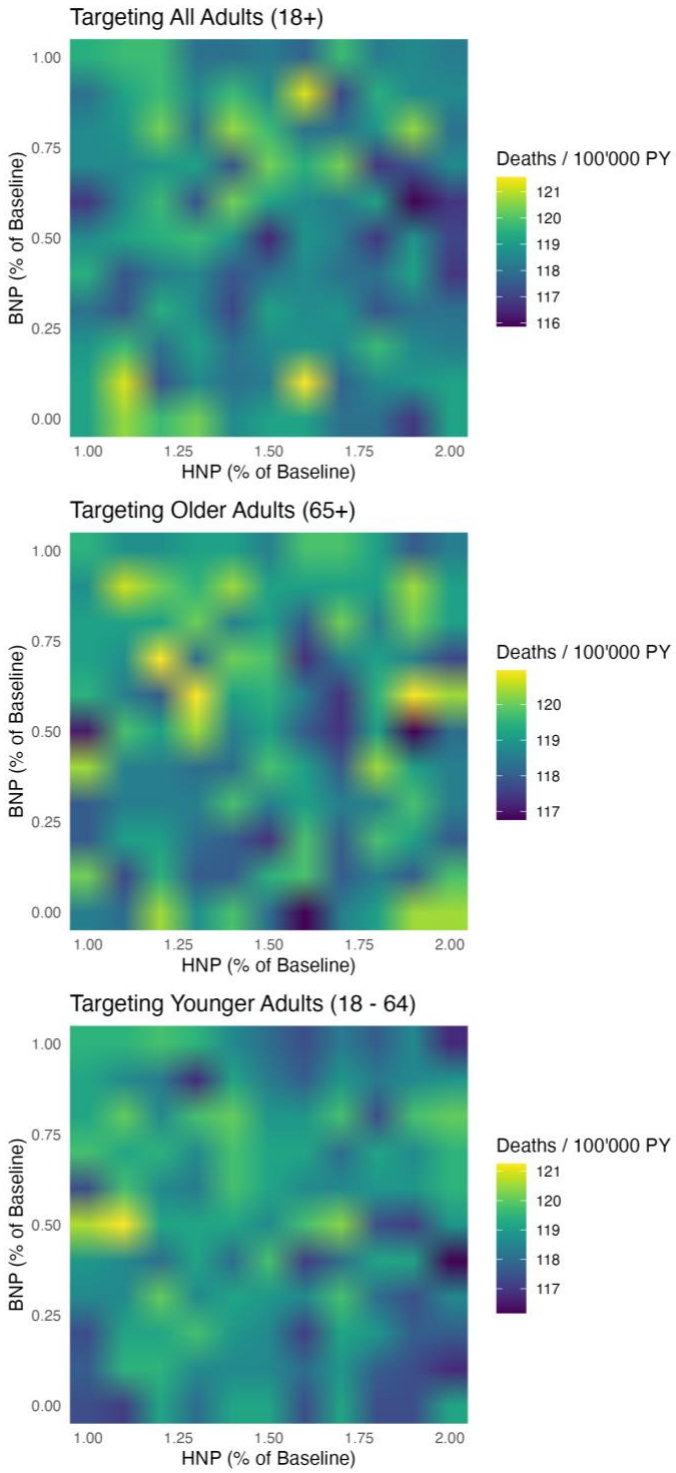
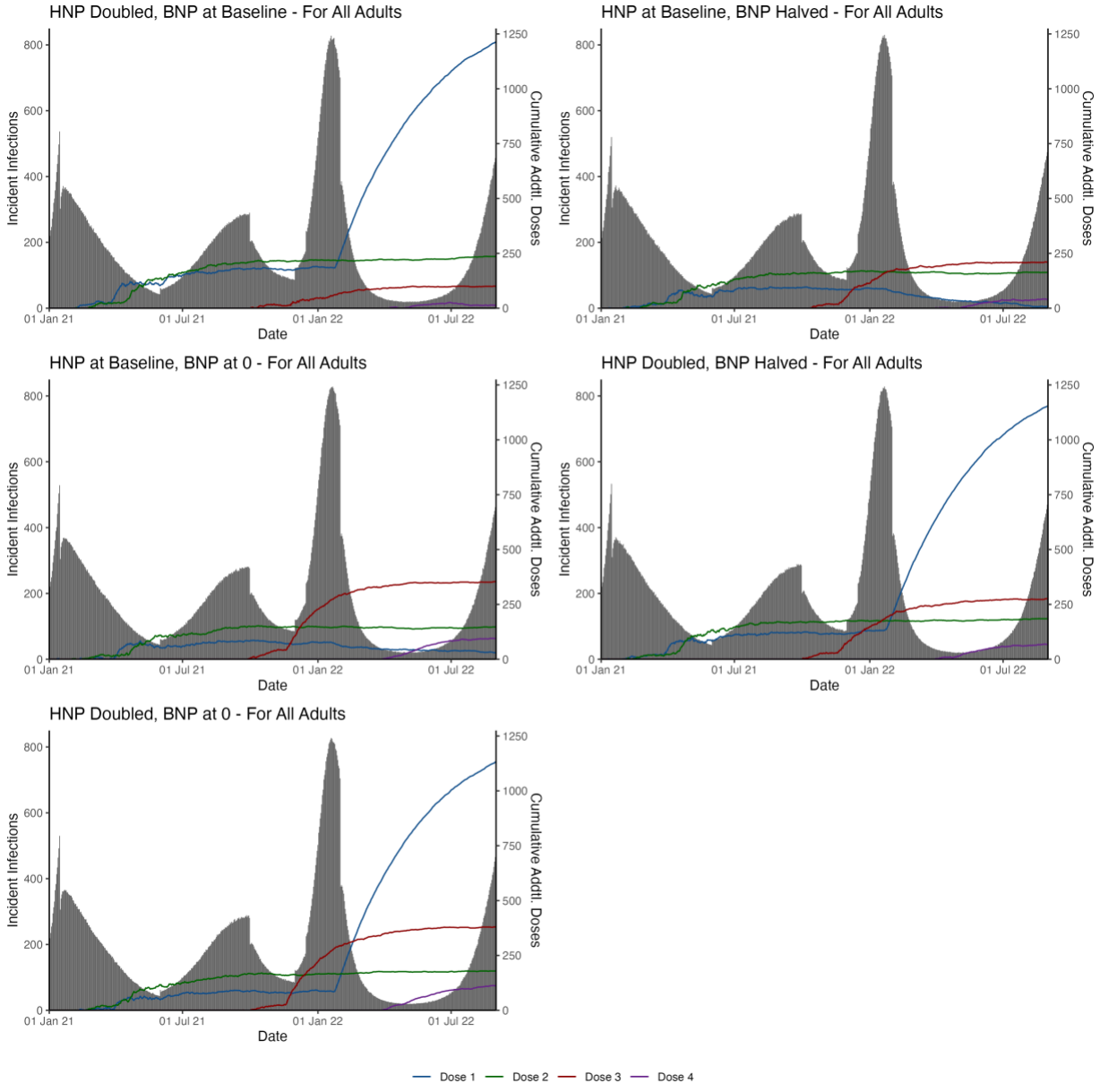


**Figure 9. Epidemic curve vs. cumulative vaccines administered over time for select scenarios.** The grey bars represent the (median) incident infections by day (across the full population of 100'000 nodes). The coloured lines represent the difference between the (median) cumulative number of vaccine doses administered across all age groups in the scenario of interest and the corresponding (median) number from the reference scenario, as of each point in time.



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# APPENDIX

**Table A1. Proportion of adult population vaccinated by dose and age group for select scenarios, with simulation intervals.**

| Scenario | | | Ages 18 - 49 | | | Ages 50 - 64 | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Targeting** | **Hospitalization Nudge Prob.** | **Breakthrough Nudge Prob.** | Dose 1 | Dose 2 | Dose 3 | Dose 1 | Dose 2 | Dose 3 | Dose 4 |
| | | | *% (50% SI)* | *% (50% SI)* | *% (50% SI)* | *% (50% SI)* | *% (50% SI)* | *% (50% SI)* | *% (50% SI)* |
| - | Reference | Reference | 71.5 (71.4, 71.6) | 62.5 (62.3, 62.6) | 18.1 (18.0, 18.2) | 71.5 (71.4, 71.6) | 62.5 (62.3, 62.6) | 34.3 (34.1, 34.6) | 7.4 (7.3, 7.6) |
| All Adults (18+) | 200% of Reference | Reference | 73.1 (73.0, 73.2) | 62.5 (62.4, 62.7) | 18.1 (18.0, 18.2) | 73.1 (73.0, 73.2) | 62.5 (62.4, 62.7) | 34.3 (34.1, 34.7) | 7.4 (7.2, 7.6) |
| | Reference | 50% of Reference | 71.5 (71.4, 71.6) | 62.5 (62.3, 62.6) | 18.3 (18.1, 18.4) | 71.5 (71.4, 71.6) | 62.5 (62.3, 62.6) | 34.6 (34.4, 34.9) | 7.5 (7.4, 7.6) |
| | Reference | 0% of Reference | 71.5 (71.4, 71.7) | 62.5 (62.4, 62.7) | 18.4 (18.3, 18.6) | 71.5 (71.4, 71.7) | 62.5 (62.4, 62.7) | 35.0 (34.7, 35.3) | 7.7 (7.6, 7.8) |
| | 200% of Reference | 50% of Reference | 73.0 (72.9, 73.2) | 62.5 (62.4, 62.6) | 18.3 (18.1, 18.4) | 73.0 (72.9, 73.2) | 62.5 (62.4, 62.6) | 34.7 (34.4, 34.9) | 7.6 (7.4, 7.7) |
| | 200% of Reference | 0% of Reference | 73.1 (72.9, 73.1) | 62.5 (62.4, 62.7) | 18.4 (18.3, 18.6) | 73.1 (72.9, 73.1) | 62.5 (62.4, 62.7) | 35.0 (34.8, 35.3) | 7.7 (7.6, 7.9) |
| Older Adults (65+) | 200% of Reference | Reference | 71.5 (71.4, 71.7) | 62.5 (62.3, 62.7) | 18.1 (17.9, 18.3) | 71.5 (71.4, 71.7) | 62.5 (62.3, 62.7) | 34.3 (34.1, 34.6) | 7.4 (7.3, 7.6) |
| | Reference | 50% of Reference | 71.5 (71.4, 71.8) | 62.6 (62.4, 62.8) | 18.1 (18.0, 18.3) | 71.5 (71.4, 71.8) | 62.6 (62.4, 62.8) | 34.3 (34.1, 34.8) | 7.4 (7.3, 7.6) |
| | Reference | 0% of Reference | 71.5 (71.4, 71.6) | 62.5 (62.4, 62.7) | 18.1 (18.0, 18.3) | 71.5 (71.4, 71.6) | 62.5 (62.4, 62.7) | 34.3 (34.0, 34.6) | 7.4 (7.2, 7.5) |
| | 200% of Reference | 50% of Reference | 71.5 (71.4, 71.7) | 62.5 (62.3, 62.6) | 18.1 (18.0, 18.3) | 71.5 (71.4, 71.7) | 62.5 (62.3, 62.6) | 34.3 (34.0, 34.6) | 7.4 (7.3, 7.5) |
| | 200% of Reference | 0% of Reference | 71.5 (71.4, 71.7) | 62.5 (62.4, 62.7) | 18.1 (18.0, 18.2) | 71.5 (71.4, 71.7) | 62.5 (62.4, 62.7) | 34.4 (34.1, 34.7) | 7.4 (7.3, 7.6) |
| Younger Adults (18 - 64) | 200% of Reference | Reference | 73.1 (72.9, 73.2) | 62.5 (62.4, 62.6) | 18.1 (18.0, 18.3) | 73.1 (72.9, 73.2) | 62.5 (62.4, 62.6) | 34.3 (34.1, 34.6) | 7.5 (7.3, 7.6) |
| | Reference | 50% of Reference | 71.5 (71.4, 71.7) | 62.5 (62.3, 62.7) | 18.3 (18.1, 18.5) | 71.5 (71.4, 71.7) | 62.5 (62.3, 62.7) | 34.6 (34.4, 35.0) | 7.6 (7.4, 7.7) |
| | Reference | 0% of Reference | 71.5 (71.3, 71.7) | 62.5 (62.3, 62.7) | 18.4 (18.2, 18.6) | 71.5 (71.3, 71.7) | 62.5 (62.3, 62.7) | 35.0 (34.7, 35.3) | 7.7 (7.5, 7.8) |
| | 200% of Reference | 50% of Reference | 73.0 (72.9, 73.2) | 62.5 (62.4, 62.7) | 18.3 (18.1, 18.4) | 73.0 (72.9, 73.2) | 62.5 (62.4, 62.7) | 34.6 (34.4, 35.0) | 7.5 (7.4, 7.7) |
| | 200% of Reference | 0% of Reference | 73.1 (72.9, 73.2) | 62.5 (62.4, 62.6) | 18.5 (18.2, 18.6) | 73.1 (72.9, 73.2) | 62.5 (62.4, 62.6) | 35.0 (34.8, 35.3) | 7.7 (7.5, 7.9) |

| Scenario | | | Ages 65+ | | | |
|---|---|---|---|---|---|---|
| **Targeting** | **Hospitalization Nudge Probability** | **Breakthrough Nudge Probability** | Dose 1 *% (50% SI)* | Dose 2 *% (50% SI)* | Dose 3 *% (50% SI)* | Dose 4 *% (50% SI)* |
| - | Reference | Reference | 89.5 (89.3, 89.7) | 81.1 (80.9, 81.4) | 51.8 (51.4, 52.0) | 15.0 (14.9, 15.3) |
| All Adults (18+) | 200% of Reference | Reference | 90.5 (90.3, 90.7) | 81.2 (80.9, 81.4) | 51.9 (51.7, 52.1) | 15.1 (14.9, 15.3) |
| | Reference | 50% of Reference | 89.5 (89.4, 89.7) | 81.1 (80.9, 81.4) | 52.0 (51.7, 52.3) | 15.2 (15.0, 15.3) |
| | Reference | 0% of Reference | 89.6 (89.4, 89.7) | 81.1 (80.9, 81.4) | 52.3 (52.0, 52.5) | 15.4 (15.2, 15.6) |
| | 200% of Reference | 50% of Reference | 90.4 (90.3, 90.6) | 81.1 (80.9, 81.4) | 52.1 (51.8, 52.4) | 15.3 (15.1, 15.5) |
| | 200% of Reference | 0% of Reference | 90.5 (90.3, 90.6) | 81.1 (81.0, 81.3) | 52.2 (51.9, 52.6) | 15.3 (15.2, 15.6) |
| Older Adults (65+) | 200% of Reference | Reference | 90.4 (90.2, 90.5) | 81.2 (80.9, 81.5) | 51.8 (51.6, 52.3) | 15.1 (14.9, 15.3) |
| | Reference | 50% of Reference | 89.6 (89.4, 89.7) | 81.1 (80.9, 81.4) | 52.1 (51.8, 52.4) | 15.2 (15.0, 15.4) |
| | Reference | 0% of Reference | 89.5 (89.3, 89.7) | 81.1 (80.9, 81.4) | 52.1 (51.9, 52.4) | 15.3 (15.1, 15.5) |
| | 200% of Reference | 50% of Reference | 90.3 (90.2, 90.6) | 81.1 (80.9, 81.4) | 52.0 (51.7, 52.4) | 15.2 (15.0, 15.4) |
| | 200% of Reference | 0% of Reference | 90.4 (90.2, 90.6) | 81.1 (81.0, 81.5) | 52.2 (52.0, 52.5) | 15.4 (15.2, 15.6) |
| Younger Adults (18 - 64) | 200% of Reference | Reference | 89.6 (89.4, 89.8) | 81.1 (80.9, 81.3) | 51.8 (51.5, 52.1) | 15.0 (14.8, 15.2) |
| | Reference | 50% of Reference | 89.5 (89.4, 89.7) | 81.1 (80.9, 81.4) | 51.8 (51.5, 52.2) | 15.1 (14.9, 15.3) |
| | Reference | 0% of Reference | 89.6 (89.4, 89.7) | 81.2 (81.0, 81.4) | 51.8 (51.6, 52.1) | 15.0 (14.9, 15.2) |
| | 200% of Reference | 50% of Reference | 89.6 (89.5, 89.8) | 81.1 (80.9, 81.4) | 51.9 (51.6, 52.3) | 15.0 (14.9, 15.3) |
| | 200% of Reference | 0% of Reference | 89.6 (89.5, 89.8) | 81.1 (80.9, 81.4) | 51.8 (51.6, 52.2) | 15.0 (14.9, 15.2) |

**Table A2.** Cumulative infections and infections averted by end of simulation for select scenarios, with simulation intervals.

| Scenario | | | Total Infections per 100'000 PY | Infections Averted per 100'000 PY | Percent of Infections Averted | Infections Averted per Addtl. Dose |
|---|---|---|---|---|---|---|
| **Targeting** | **Hospitalization Nudge Prob.** | **Breakthrough Nudge Prob.** | *n (50% SI)* | *n (50% SI)* | *% (50% SI)* | *n (50% SI)* |
| - | Reference | Reference | 67'746.4 (66'937.9, 68'534.7) | - | - | - |
| All Adults (18+) | 200% of Reference | Reference | 67'256.6 (66'269.6, 67'980.8) | 489.8 (-234.4, 1'476.8) | 0.7 (-0.3, 2.2) | 0.5 (-0.4, 1.9) |
| | Reference | 50% of Reference | 67'701.8 (66'528.3, 68'461.8) | 44.6 (-715.4, 1'218.1) | 0.1 (-1.1, 1.8) | 0.1 (-5.2, 5.1) |
| | Reference | 0% of Reference | 67'632.6 (66'830.5, 68'605.8) | 113.8 (-859.4, 915.9) | 0.2 (-1.3, 1.4) | 0.2 (-2.9, 2.6) |
| | 200% of Reference | 50% of Reference | 67'531.7 (66'569.6, 68'487.0) | 214.7 (-740.6, 1'176.8) | 0.3 (-1.1, 1.7) | 0.2 (-1.0, 1.0) |
| | 200% of Reference | 0% of Reference | 67'270.7 (66'320.7, 68'237.9) | 475.7 (-491.5, 1'425.7) | 0.7 (-0.7, 2.1) | 0.3 (-0.5, 1.3) |
| Older Adults (65+) | 200% of Reference | Reference | 67'435.0 (66'429.5, 68'505.1) | 311.4 (-758.7, 1'316.9) | 0.5 (-1.1, 1.9) | 0.4 (-5.1, 5.0) |
| | Reference | 50% of Reference | 67'542.2 (66'697.9, 68'636.7) | 204.2 (-890.3, 1'048.5) | 0.3 (-1.3, 1.5) | 0.4 (-4.1, 4.7) |
| | Reference | 0% of Reference | 67'638.6 (66'636.8, 68'435.9) | 107.8 (-689.5, 1'109.6) | 0.2 (-1.0, 1.6) | 0.0 (-7.1, 4.6) |
| | 200% of Reference | 50% of Reference | 67'786.2 (66'827.2, 68'672.3) | -39.8 (-925.9, 919.2) | -0.1 (-1.4, 1.4) | -0.2 (-6.7, 4.2) |
| | 200% of Reference | 0% of Reference | 67'412.9 (66'600.4, 68'459.6) | 333.5 (-713.2, 1'146.0) | 0.5 (-1.1, 1.7) | 1.2 (-2.0, 5.8) |
| Younger Adults (18 - 64) | 200% of Reference | Reference | 67'358.1 (66'325.1, 68'409.7) | 388.3 (-663.3, 1'421.3) | 0.6 (-1.0, 2.1) | 0.6 (-0.9, 2.3) |
| | Reference | 50% of Reference | 67'702.4 (66'601.6, 68'403.4) | 44.0 (-657.0, 1'144.8) | 0.1 (-1.0, 1.7) | 0.3 (-2.2, 3.5) |
| | Reference | 0% of Reference | 67'527.5 (66'499.1, 68'492.8) | 218.9 (-746.4, 1'247.3) | 0.3 (-1.1, 1.8) | 0.1 (-3.7, 3.5) |
| | 200% of Reference | 50% of Reference | 67'182.0 (66'253.0, 68'173.5) | 564.4 (-427.1, 1'493.4) | 0.8 (-0.6, 2.2) | 0.5 (-0.5, 1.7) |
| | 200% of Reference | 0% of Reference | 67'294.0 (66'546.1, 68'037.6) | 452.4 (-291.2, 1'200.3) | 0.7 (-0.4, 1.8) | 0.4 (-0.4, 1.7) |

**Table A3.** Cumulative deaths and deaths averted by end of simulation for select scenarios, with simulation intervals.

| Scenario | | | Total Deaths per 100'000 PY | Deaths Averted per 100'000 PY | Percent of Deaths Averted | Deaths Averted per Addtl. Dose |
|---|---|---|---|---|---|---|
| **Targeting** | **Hospitalization Nudge Prob.** | **Breakthrough Nudge Prob.** | *n (50% SI)* | *n (50% SI)* | *% (50% SI)* | *n (50% SI)* |
| - | Reference | Reference | 119.5 (113.2, 124.0) | - | - | - |
| All Adults (18+) | 200% of Reference | Reference | 118.3 (113.8, 124.0) | 1.2 (-4.5, 5.7) | 1.0 (-3.8, 4.8) | 0.0 (0.0, 0.0) |
| | Reference | 50% of Reference | 118.6 (113.2, 124.1) | 0.9 (-4.6, 6.3) | 0.8 (-3.9, 5.3) | 0.0 (0.0, 0.0) |
| | Reference | 0% of Reference | 119.2 (112.0, 124.1) | 0.3 (-4.6, 7.5) | 0.3 (-3.9, 6.3) | 0.0 (0.0, 0.0) |
| | 200% of Reference | 50% of Reference | 117.1 (112.0, 123.4) | 2.4 (-3.9, 7.5) | 2.0 (-3.3, 6.3) | 0.0 (0.0, 0.0) |
| | 200% of Reference | 0% of Reference | 119.2 (113.2, 124.1) | 0.3 (-4.6, 6.3) | 0.3 (-3.9, 5.3) | 0.0 (0.0, 0.0) |
| Older Adults (65+) | 200% of Reference | Reference | 118.6 (114.4, 123.5) | 0.9 (-4.0, 5.1) | 0.8 (-3.4, 4.3) | 0.0 (0.0, 0.0) |
| | Reference | 50% of Reference | 117.1 (111.2, 121.1) | 2.4 (-1.6, 8.3) | 2.0 (-1.4, 6.9) | 0.0 (0.0, 0.0) |
| | Reference | 0% of Reference | 118.6 (113.8, 123.5) | 0.9 (-4.0, 5.7) | 0.8 (-3.4, 4.8) | 0.0 (0.0, 0.0) |
| | 200% of Reference | 50% of Reference | 118.3 (112.0, 125.1) | 1.2 (-5.6, 7.5) | 1.0 (-4.8, 6.3) | 0.0 (0.0, 0.0) |
| | 200% of Reference | 0% of Reference | 120.4 (113.6, 124.7) | -0.9 (-5.2, 5.9) | -0.8 (-4.4, 4.9) | 0.0 (0.0, 0.0) |
| Younger Adults (18 - 64) | 200% of Reference | Reference | 116.8 (112.4, 123.4) | 2.7 (-3.9, 7.1) | 2.3 (-3.3, 5.9) | 0.0 (0.0, 0.0) |
| | Reference | 50% of Reference | 120.7 (114.4, 126.5) | -1.2 (-7.0, 5.1) | -1.0 (-5.9, 4.3) | 0.0 (0.0, 0.0) |
| | Reference | 0% of Reference | 117.4 (112.0, 124.0) | 2.1 (-4.5, 7.5) | 1.8 (-3.8, 6.3) | 0.0 (0.0, 0.0) |
| | 200% of Reference | 50% of Reference | 118.9 (113.2, 124.0) | 0.6 (-4.5, 6.3) | 0.5 (-3.8, 5.3) | 0.0 (0.0, 0.0) |
| | 200% of Reference | 0% of Reference | 119.2 (113.8, 124.0) | 0.3 (-4.5, 5.7) | 0.3 (-3.8, 4.8) | 0.0 (0.0, 0.0) |