Supplementary information

COVID-19 vaccine booster strategies in light of emerging viral variants: Frequency, timing, and target groups

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1. Supplementary methods

1.1. Disease prognosis and effect of variant properties

Our individual-based model, OpenCOVID, is a dynamic stochastic discrete-time model of SARS-CoV-2 transmission and COVID-19 disease progression and response.[1] The model simulates viral transmission between infectious and susceptible individuals that come in contact through an age-structured, small-world network. The probability of transmission in each exposure stage is influenced by the infectiousness of the infected individual, the immunity of the susceptible individual (acquired through previous infection and/or through vaccination), and a background seasonality pattern (reflecting a larger proportion of contacts being in closer contact indoors as the temperatures became cooler). Infectiousness is a function of variant infectivity and time since infection. Once infected, a latency period is followed by a pre-symptomatic stage, after which an individual can experience asymptomatic, mild, or severe disease. Severe cases can lead to hospitalisation, intensive care unit admission, and ultimately death (see Supplementary Table S1 for further details on prognosis probabilities by age, following infection with SARS-CoV-2 Omicron variant). Recovery after infection leads to development of immunity. This immunity is assumed to wane over time as illustrated in Figure S1, with the risk of new infection depending on the probability of exposure and properties of existing and potential novel SARS-COV-2 variants (i.e., infectiousness and immune evading profile). The model has the capacity to represent a number of containment measures, including non-pharmaceutical interventions such as physical distancing and facemask usage, testing strategies such as test-diagnose, isolate or quarantine, mass testing, and contact tracing, and pharmaceutical interventions, such as vaccination and treatment. A detailed description of the OpenCOVID model is provided in [1,2]. Open access source code for the OpenCOVID model is publicly available at https://github.com/SwissTPH/OpenCOVID.

1.2. Vaccine-induced and naturally acquired SARS-CoV-2 immunity profiles

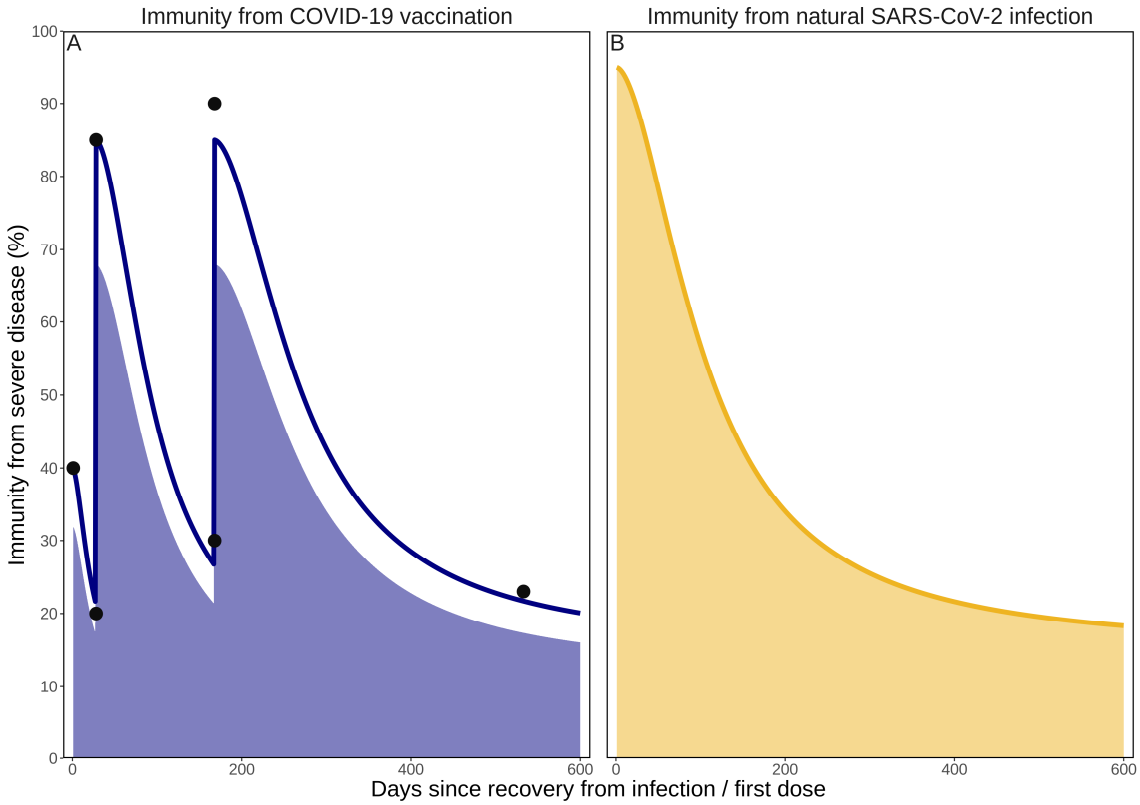

Figure S1: Profiles of COVID-19 vaccine induced immunity (panel A) and naturally acquired immunity following infection with SARS-CoV-2 (panel B) as described in the *Vaccination strategy* section of the *Methods* in the main text. Points indicate initial vaccine efficacy with exponential decay, with subsequent booster dose efficiency rebounding with an identical decay (based on [3]).

1.3. Disease prognosis and effect of variant properties

The probabilities of 1) a symptomatic case developing severe disease, 2) a severe case becoming critical, and 3) a critical case ultimately leading to death are defined as functions of age (Table S1). Additionally, individuals with severe comorbidities also experience an increased probability in developing severe disease. In our simulations, about 33% of the total population is considered most vulnerable, i.e. at highest risk of developing severe disease, which includes those 60 years and older or those with one or more severe comorbidities. In this study we used continuous functions fitted to the discrete probabilities reported in [4], updated to represent the additional risk of severe disease from infection with the SARS-CoV-2 Omicron variant (B.1.1.529)[5-7]. Table S2 shows the multiplicative factors used to represent Omicron, relative to wild type SARS-CoV-2 for which the prognosis probabilities in [4] were estimated. In addition to age-related risk, the probability that an infected individual will develop severe symptoms can also be scaled by the severity factor corresponding to the viral variant to which they were exposed.

For vaccinated individuals that become infected (noting that the infection-blocking action of the vaccine reduces the probability of infection), the probability of developing severe disease is reduced by the disease-blocking action of the vaccine. The level to which the probability of severe disease is reduced is dependent upon the level of immunity at the time of infection. Vaccine-induced immunity is assumed to wane over time (Figure S1) and can be further decreased if exposed to a variant with immune-evading capacity.

Table S1: Prognosis probabilities by age, following infection with SARS-CoV-2 Omicron variant

Age group (years)	Asymptomatic	Mild disease	Severe disease	Critical disease	Death
0–>10	33.00%	67.00%	<0.01%	<0.01%	<0.01%
10–>20	33.00%	66.98%	0.02%	<0.01%	<0.01%
20–>30	32.97%	66.81%	0.21%	0.01%	<0.01%
30–>40	32.94%	66.52%	0.51%	0.03%	<0.01%
40–>50	32.65%	64.35%	2.77%	0.24%	<0.01%
50–>60	31.73%	58.00%	8.91%	1.36%	0.01%
60–>70	29.54%	45.44%	18.89%	5.99%	0.14%
70–>80	26.74%	33.23%	22.64%	15.21%	2.17%
80–90+	24.22%	24.94%	15.66%	21.55%	13.63%

Table S2: Infectivity and severity of SARS-CoV-2 variants of concern (VOC) relative to the previously dominant variant

VOC	Lineage name	Date of designation[8]	Variant overtaken	Infectivity	Severity
Wild-type		31 Dec 2019			
D614	D614	15 Mar 2020	Wild-type	1.00	1.00
G614	G614		D614	3.00[2]	1.00
Alpha	B.1.1.7	18 Dec 2020	G614	1.64 (95% CI 1.32–2.04)[4]	1.67 (95% CI 1.34–2.09)[4]
Delta	B.1.617.2	11 May 2021	Alpha	1.50[5]–6.00[6]	Hospitalisation:1.85 (95% CI 1.39–2.47)[7] ICU admission: 2.34 (95% CI 1.64–3.31)[9] Death: 1.32 (95% CI 0.47–2.30)[9]
Omicron	B.1.1.529	26 Nov 2021	Delta	3.20 (95% CI 2.00–5.00)[10]	Hospitalisation among 60–69-year-olds: 0.75[11]

1.4. Seasonality

Seasonality is assumed to follow a scaled cosine function, oscillating between a minimum point (-1), representing minimum seasonal forcing during the peak summer period, and maximum seasonal forcing during the peak winter period (1). The best estimate for the seasonal scaling factor, 0.3, was taken from a previous study assessing the COVID-19 epidemic in Switzerland.[1] This previous study simultaneously fit this seasonal scaling factor parameter along with several other parameters to align the OpenCOVID model to epidemiological data. To assess the effect of the seasonal scaling factor on model outcomes, two additional values for the peak summer effect were modelled in a sensitivity analysis (see Figure 5 from the main text): 0.2 (yellow curve, representing a less seasonal, more perennial setting) and 0.4 (green curve, representing a more seasonal setting).

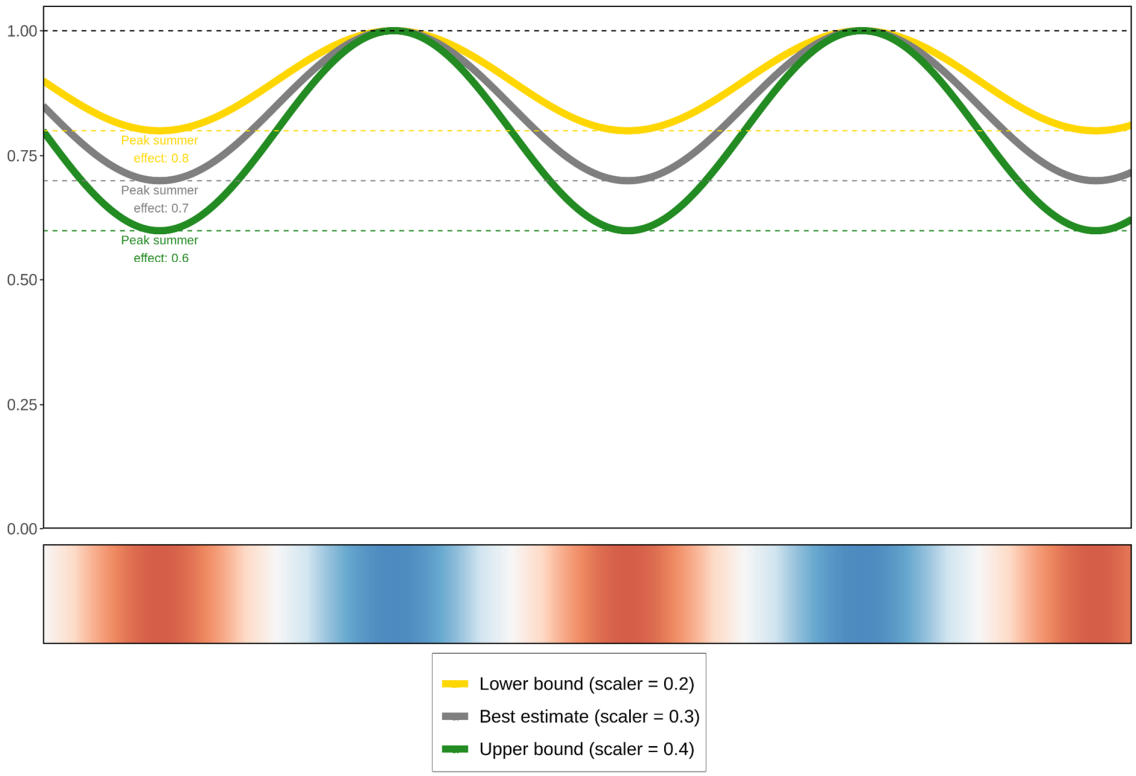

Figure S2: Impact of seasonal forcing scalers (best estimate (grey curve), lower bound (yellow curve), and upper bound (green curve)) on SARS-CoV-2 infectiousness per contact over a two year period. Seasonality is illustrated in the bottom row where red shading indicates the warmer spring and summer seasons, blue the cooler fall and winter seasons, and white the seasonal transition periods.

2. Supplementary results

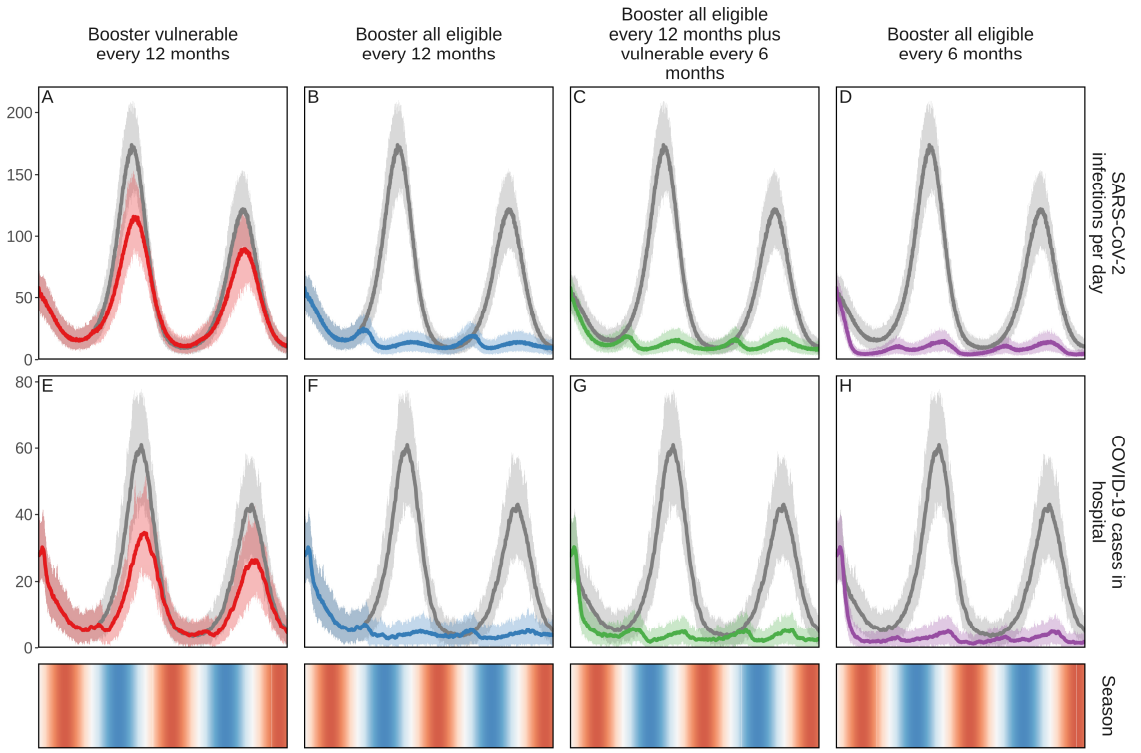

Figure S3A: Projected impact of COVID-19 vaccine boosters on daily SARS-CoV-2 infections and COVID-19-related cases in hospital. The simulation was for just over a two-year period in a population of 100,000 individuals. Those who were modelled as having previously received vaccine doses one and two, including 93% of those 60+ or with comorbidities, 90% of 50−59 year olds, 80% of 30−49 year olds, and 75% of 5−29 year olds, are eligible to receive first-generation COVID-19 vaccine boosters. Populations who received boosters every twelve or six months are aggregated into two groups, (1) those most vulnerable (60 years and older or persons with comorbidities) and (2) all eligible (five years and older). Each vaccine scenario curve is plotted alongside the baseline scenario whereby no vaccine booster doses were administered (grey curves). In these simulations, no new SARS-CoV-2 variants emerged, and the same infectiousness and severity of the Omicron variant was assumed. Shaded areas represent the stochastic uncertainty surrounding projections. Cumulative number and timing of vaccine doses are shown for each scenario. Seasonality is illustrated in the bottom row where red shading indicates the warmer spring and summer seasons, blue the cooler fall and winter seasons, and white the seasonal transition periods. This figure is an extension of Figure 1 from the main text.

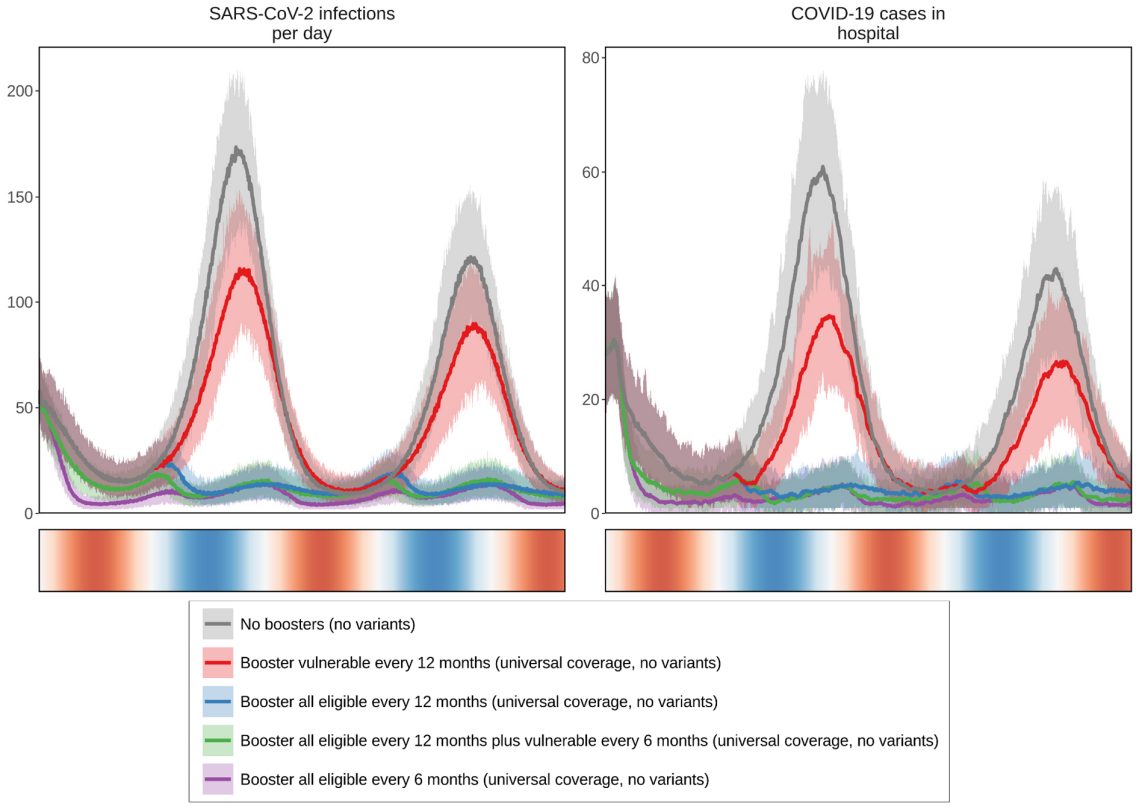

Figure S3B: Projected daily impact on SARS-CoV-2 infections and COVID-19-related cases in hospital over a two-year period in a simulated population of 100,000 individuals. Those who were modelled as having previously received vaccine doses one and two, including 93% of those 60+ or with comorbidities, 90% of 50−59 year olds, 80% of 30−49 year olds, and 75% of 5−29 year olds, are eligible to receive first-generation COVID-19 vaccine boosters. Populations who received boosters every twelve or six months are aggregated into two groups, (1) those most vulnerable (60 years and older or persons with comorbidities) and (2) all eligible (five years and older). Vaccine scenario curves are plotted alongside a baseline scenario (grey curve) whereby no vaccine booster doses were administered (grey curves). Universal coverage of booster doses is 98% of those eligible. In these simulations, no new SARS-CoV-2 variants emerged, and the same infectiousness and severity of the Omicron variant was assumed. Shaded areas represent the stochastic uncertainty surrounding projections. Cumulative number and timing of vaccine doses are shown for each scenario. Seasonality is illustrated in the bottom row where red shading indicates the warmer spring and summer seasons, blue the cooler fall and winter seasons, and white the seasonal transition periods. This figure shows the same results as Figure S3A but with curves plotted within the same outcome panel.

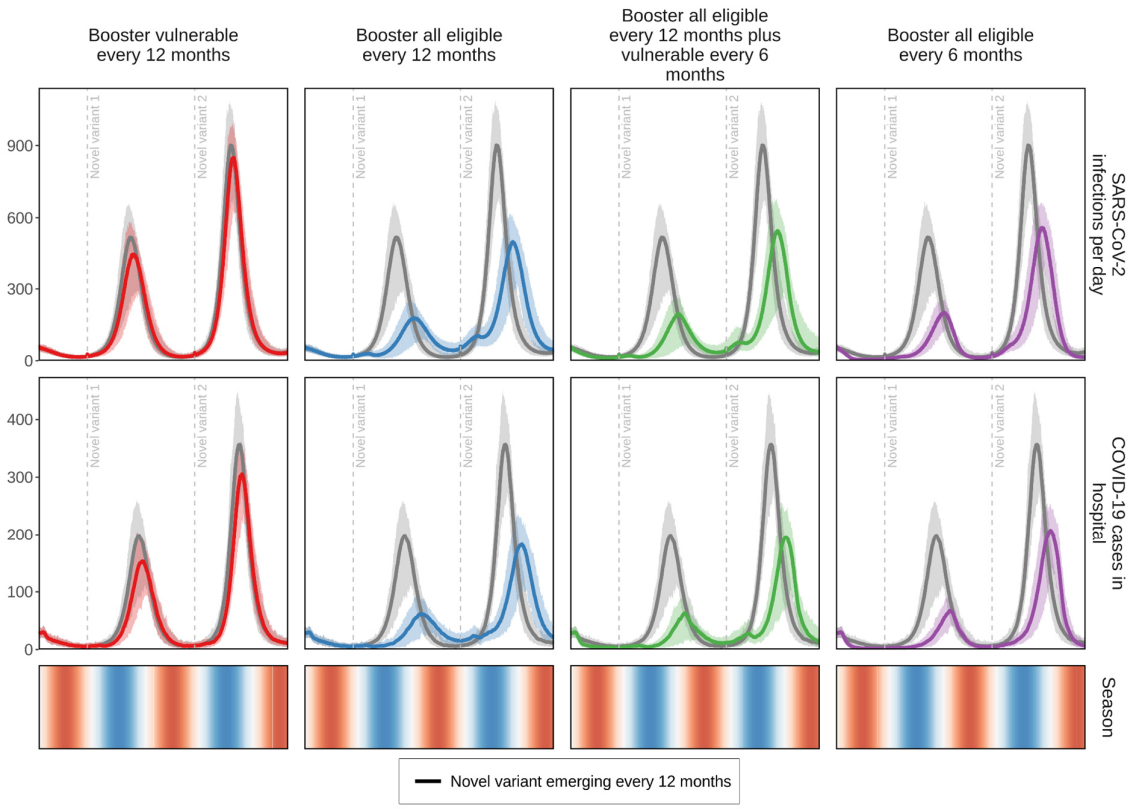

Figure S4A: Projected daily impact on SARS-CoV-2 infections and COVID-19-related hospital admissions for just over a two-year period in a simulated population of 100,000 individuals. Those who were modelled as having previously received vaccine doses one and two, including 93% of those 60+ or with comorbidities, 90% of 50−59 year olds, 80% of 30−49 year olds, and 75% of 5−29 year olds, are eligible to receive first-generation COVID-19 vaccine boosters. Populations who received boosters every twelve or six months are aggregated into two groups, (1) those most vulnerable (60 years and older or persons with comorbidities) and (2) all eligible (five years and older). Each vaccine scenario curve is plotted alongside a baseline scenario (grey curve) whereby no vaccine booster doses were administered (grey curves). Booster dose coverage is 98% of those eligible (universal coverage). Novel SARS-CoV-2 variants with 25% more infectiousness and immune evading capacity than the previously dominant variant but with the same severity as the Omicron variant emerged annually (initial emergence indicated with horizontal dashed lines). Shaded areas represent the stochastic uncertainty surrounding projections. Cumulative number and timing of vaccine doses are shown for each scenario. Seasonality is illustrated in the bottom row where red shading indicates the warmer spring and summer seasons, blue the cooler fall and winter seasons, and white the seasonal transition periods. This figure is an extension of Figure 1 from the main text.

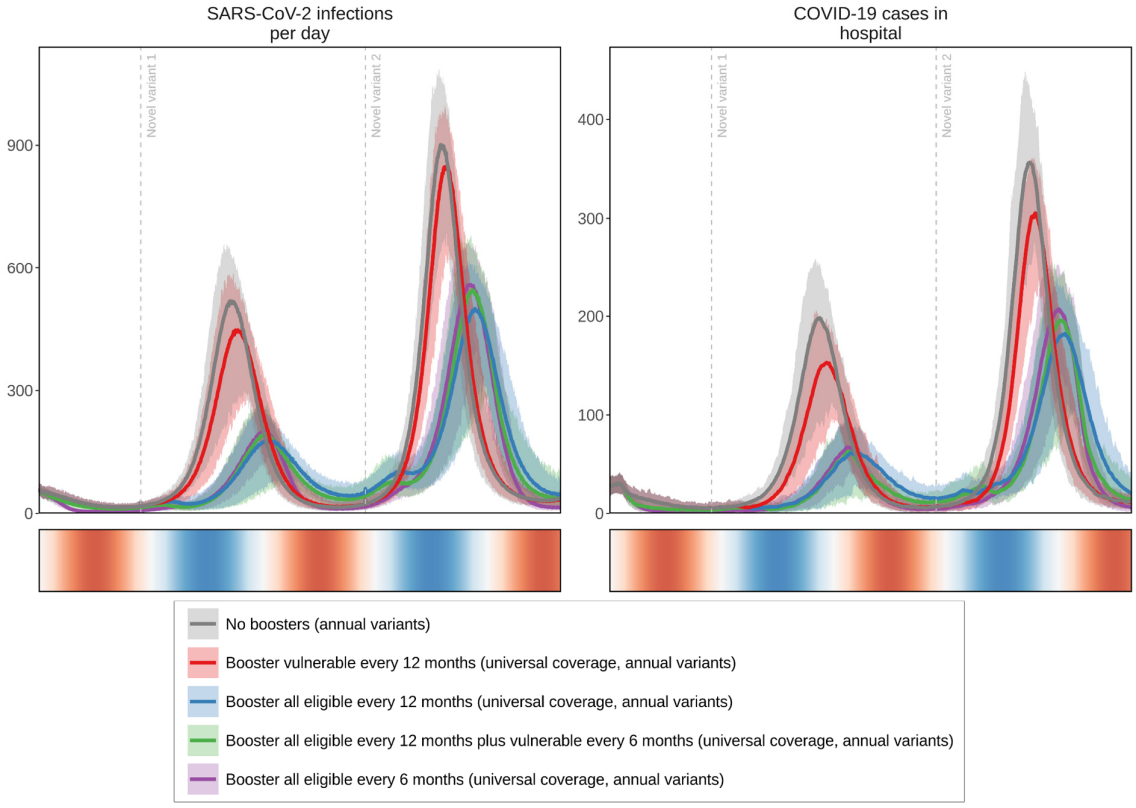

Figure S4B: Projected daily impact on SARS-CoV-2 infections and COVID-19-related cases in hospital for just over a two-year period in a simulated population of 100,000 individuals. Those who were modelled as having previously received vaccine doses one and two, including 93% of those 60+ or with comorbidities, 90% of 50−59 year olds, 80% of 30−49 year olds, and 75% of 5−29 year olds, are eligible to receive first-generation COVID-19 vaccine boosters. Populations who received boosters every twelve or six months are aggregated into two groups, (1) those most vulnerable (60 years and older or persons with comorbidities) and (2) all eligible (five years and older). Each vaccine scenario curve is plotted alongside a baseline scenario curve whereby no vaccine booster doses were administered (grey curves). Booster dose coverage is 98% of those eligible (universal coverage). Novel SARS-CoV-2 variants with 25% more infectiousness and immune evading capacity than the previously dominant variant but with the same severity as the Omicron variant emerged annually (with initial emergence indicated with horizontal dashed lines). Shaded areas represent the stochastic uncertainty surrounding projections. Cumulative number and timing of vaccine doses are shown for each scenario. Seasonality is illustrated in the bottom row where red shading indicates the warmer spring and summer seasons, blue the cooler fall and winter seasons, and white the seasonal transition periods. This figure shows the same results as Figure S4A but with curves plotted within the same outcome panel.

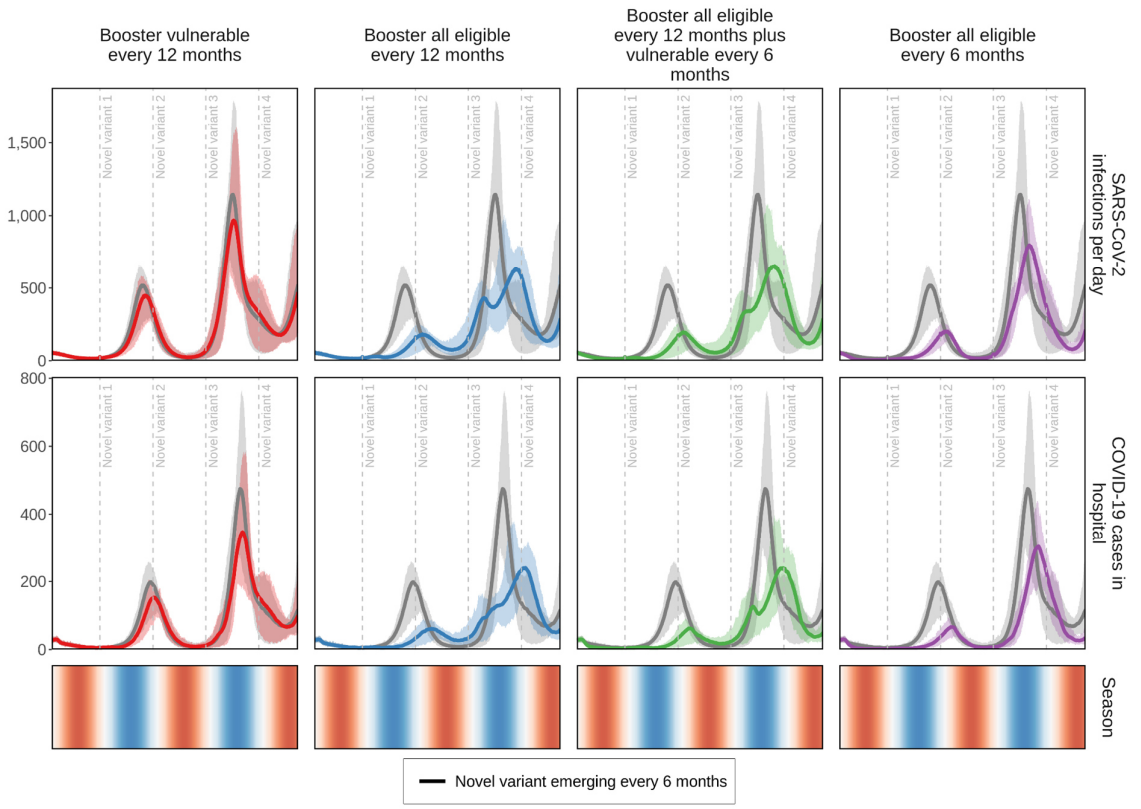

Figure S5A: Projected daily impact on SARS-CoV-2 infections and COVID-19-related hospital admissions for just over a two-year period in a simulated population of 100,000 individuals. Those who were modelled as having previously received vaccine doses one and two, including 93% of those 60+ or with comorbidities, 90% of 50−59 year olds, 80% of 30−49 year olds, and 75% of 5−29 year olds, are eligible to receive first-generation COVID-19 Populations who received boosters every twelve or six months are aggregated into two groups, (1) those most vulnerable (60 years and older or persons with comorbidities) and (2) all eligible (those aged five years and older). Each vaccine scenario curve is plotted alongside a baseline scenario (grey curve) whereby no vaccine booster doses were administered (grey curves). Booster dose coverage is 98% of those eligible (universal coverage). Novel SARS-CoV-2 variants with 25% more infectiousness and immune evading capacity than the previously dominant variant but with the same severity as the Omicron variant emerged biannually (initial emergence indicated with horizontal dashed lines). Shaded areas represent the stochastic uncertainty surrounding projections. Cumulative number and timing of vaccine doses are shown for each scenario. Seasonality is illustrated in the bottom row where red shading indicates the warmer spring and summer seasons, blue the cooler fall and winter seasons, and white the seasonal transition periods. This figure is an extension of Figure 1 from the main text.

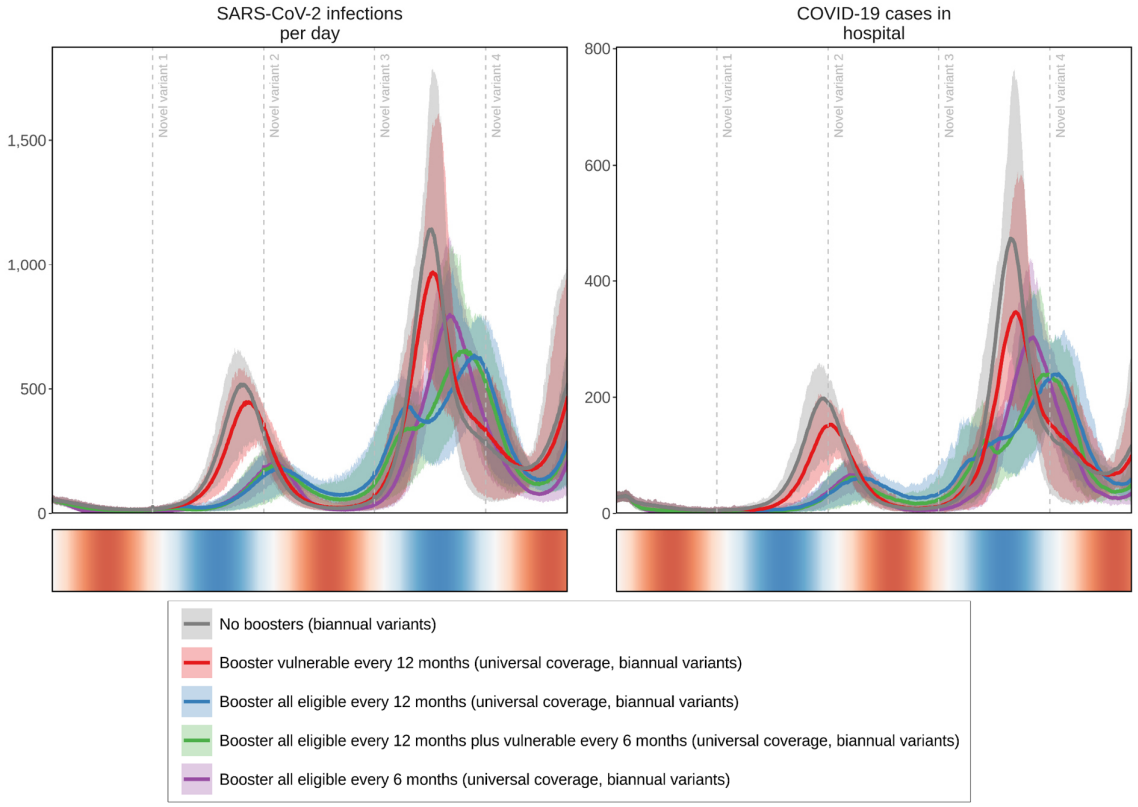

Figure S5B: Projected daily impact on SARS-CoV-2 infections and COVID-19-related hospital admissions for just over a two-year period in a simulated population of 100,000 individuals. Those who were modelled as having previously received vaccine doses one and two, including 93% of those 60+ or with comorbidities, 90% of 50−59 year olds, 80% of 30−49 year olds, and 75% of 5−29 year olds, are eligible to receive first-generation COVID-19 Populations who received boosters every twelve or six months are aggregated into two groups, (1) those most vulnerable (60 years and older or persons with comorbidities) and (2) all eligible (five years and older). Each vaccine scenario curve is plotted alongside a baseline scenario curve whereby no vaccine booster doses were administered (grey curves). Booster dose coverage is 98% of those eligible (universal coverage). Novel SARS-CoV-2 variants with 25% more infectiousness and immune evading capacity than the previously dominant variant but with the same severity as the Omicron variant emerged biannually (initial emergence indicated with horizontal dashed lines). Shaded areas represent the stochastic uncertainty surrounding projections. Cumulative number and timing of vaccine doses are shown for each scenario. Seasonality is illustrated in the bottom row where red shading indicates the warmer spring and summer seasons, blue the cooler fall and winter seasons, and white the seasonal transition periods. This figure shows the same results as Figure S5A but with curves plotted within the same outcome panel.

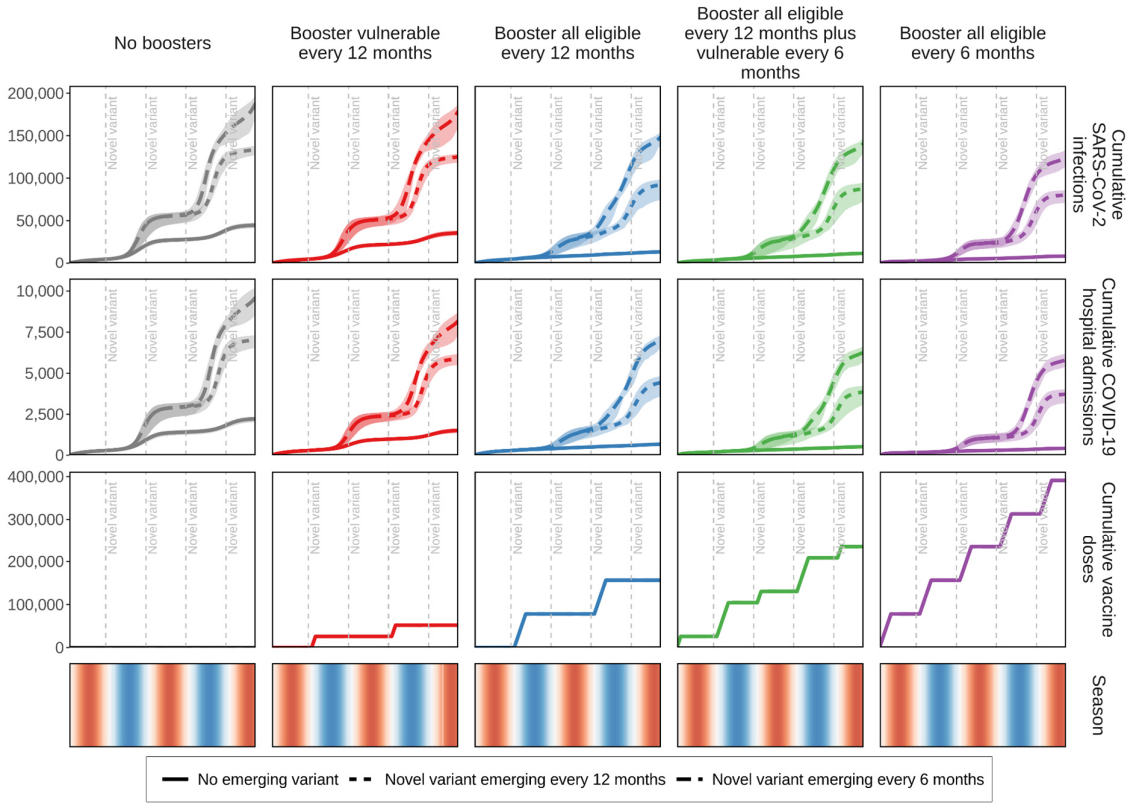

Figure S6: Cumulative projected impact on SARS-CoV-2 infections and COVID-19-related hospital admissions for just over a two-year period in a simulated population of 100,000 individuals. Those who were modelled as having previously received vaccine doses one and two, including 93% of those 60+ or with comorbidities, 90% of 50−59 year olds, 80% of 30−49 year olds, and 75% of 5−29 year olds, are eligible to receive first-generation COVID-19 We examined two main target groups who received boosters every twelve or six months, (1) those most vulnerable (60 years and older or persons with comorbidities), and (2) all eligible (five years and older). Booster dose coverage is 98% of those eligible (universal coverage). The impact of the baseline scenario (no boosters) with no vaccine boosters is represented by grey curves (left panels). It was simulated that there was either no novel emerging SARS-CoV-2 variant, assuming the same infectiousness and severity of the Omicron variant (solid curves); 25% more infectious and immune evading novel variants emerged every twelve months (short dashed curves); or every six months (long dashed curves) (timing of emerging variant indicated by initial emergence indicated with horizontal dashed lines). Shaded areas represent the stochastic uncertainty surrounding projections. Cumulative number and timing of vaccine doses are shown for each scenario. Seasonality is illustrated in the bottom row where red shading indicates the warmer spring and summer seasons, blue the cooler fall and winter seasons, and white the seasonal transition periods. This figure is an extension of Figure 2, right panels from the main text.

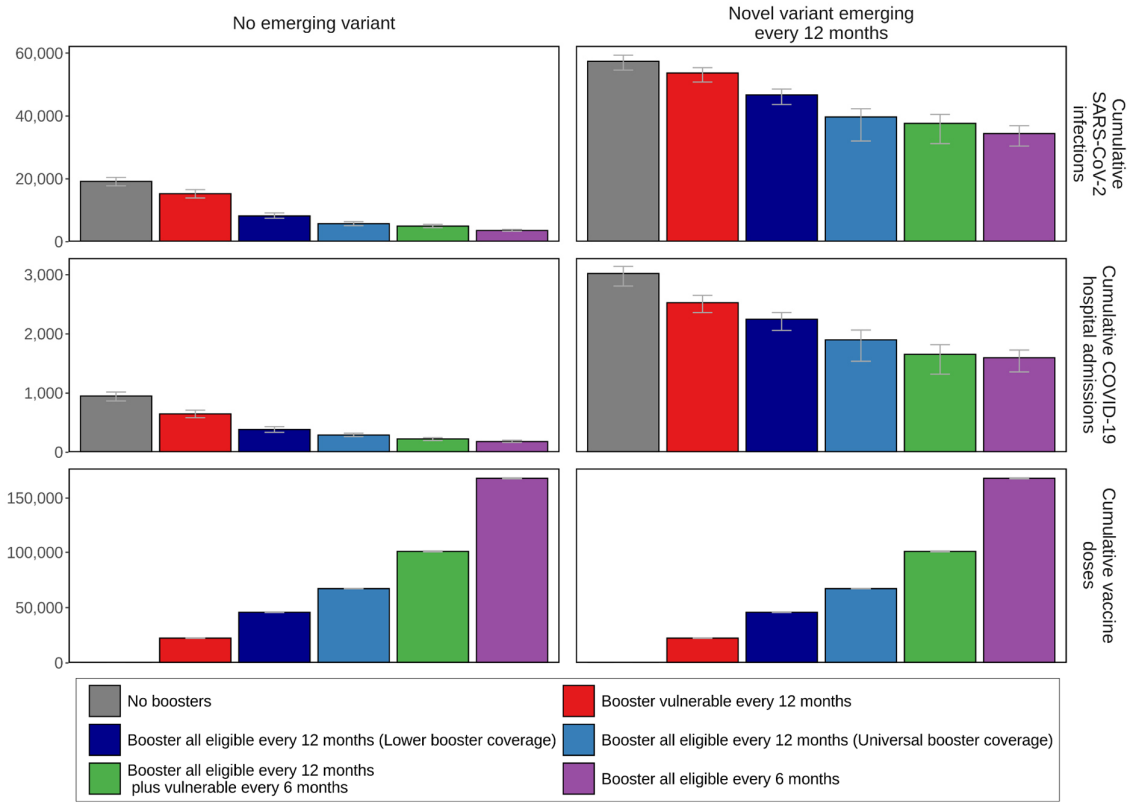

Figure S7: Cumulative projected impact on SARS-CoV-2 infections and COVID-19-related hospital admissions for just over a two-year period in a simulated population of 100,000 individuals. Those who were modelled as having previously received vaccine doses one and two, including 93% of those 60+ or with comorbidities, 90% of 50−59 year olds, 80% of 30−49 year olds, and 75% of 5−29 year olds, are eligible to receive first-generation COVID-19 Populations who received boosters every twelve or six months are aggregated into two main groups, (1) those most vulnerable (60 years and older or persons with comorbidities), and (2) all eligible (five years and older). Boosting those most vulnerable every six months includes boosting all those eligible every twelve months (green bars). Grey bars represent the impact of the baseline scenario with no vaccine boosters. Lower booster coverage was simulated as 85% coverage of those eligible to receive boosters who are most vulnerable (60 years and older or persons with comorbidities) and those 50−59 years of age, and 50% of those eligible aged 30−49 and 5−29 years. Universal booster coverage represents 98% of those eligible received booster doses. There was either no novel emerging SARS-CoV-2 variant, assuming the same infectiousness and severity of the Omicron variant (left panels), or novel variants with 25% more infectiousness and immune evading capacity emerged every twelve months (right panels). Error bars shown represent the stochastic uncertainty in model projections. This figure is a bar chart representation for cumulative impact curves from Figures 2 and 3 from the main text.

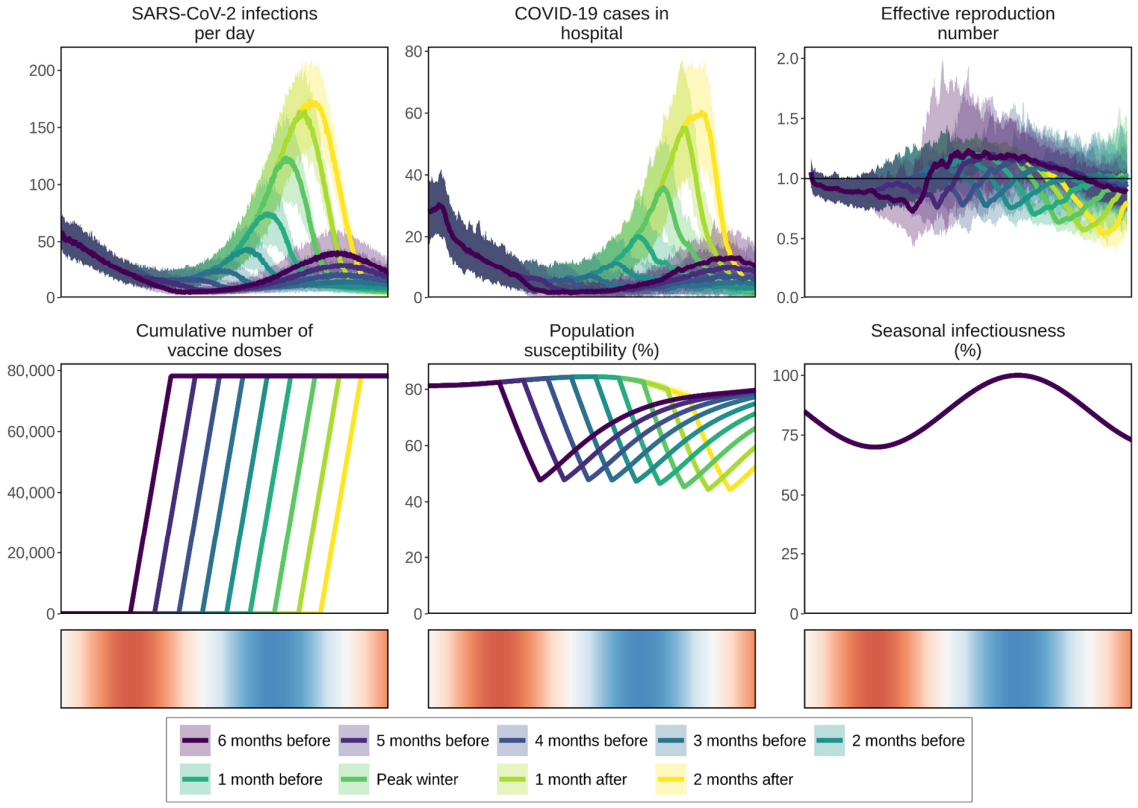

Figure S8: Projected daily impact on new COVID-19 infections, COVID-19-related hospital admissions, effective reproduction number, and population susceptibility of delivering vaccine boosters for all those eligible five years of age and older from either six months before to two months after peak winter temperatures assuming a 25% more infectious and immune evading novel variant emerges prior to the fall seasons. Shaded areas in the panels in the top row represent the stochastic uncertainty surrounding projections. Cumulative number of vaccine booster doses shown for each rollout start period. Seasonal infectiousness percentage plotted over time as a cosine function (bottom row, right panel) and illustrated in the bottom row where red shading indicates the warmer spring and summer seasons, blue the cooler fall and winter seasons, and white the seasonal transition periods.

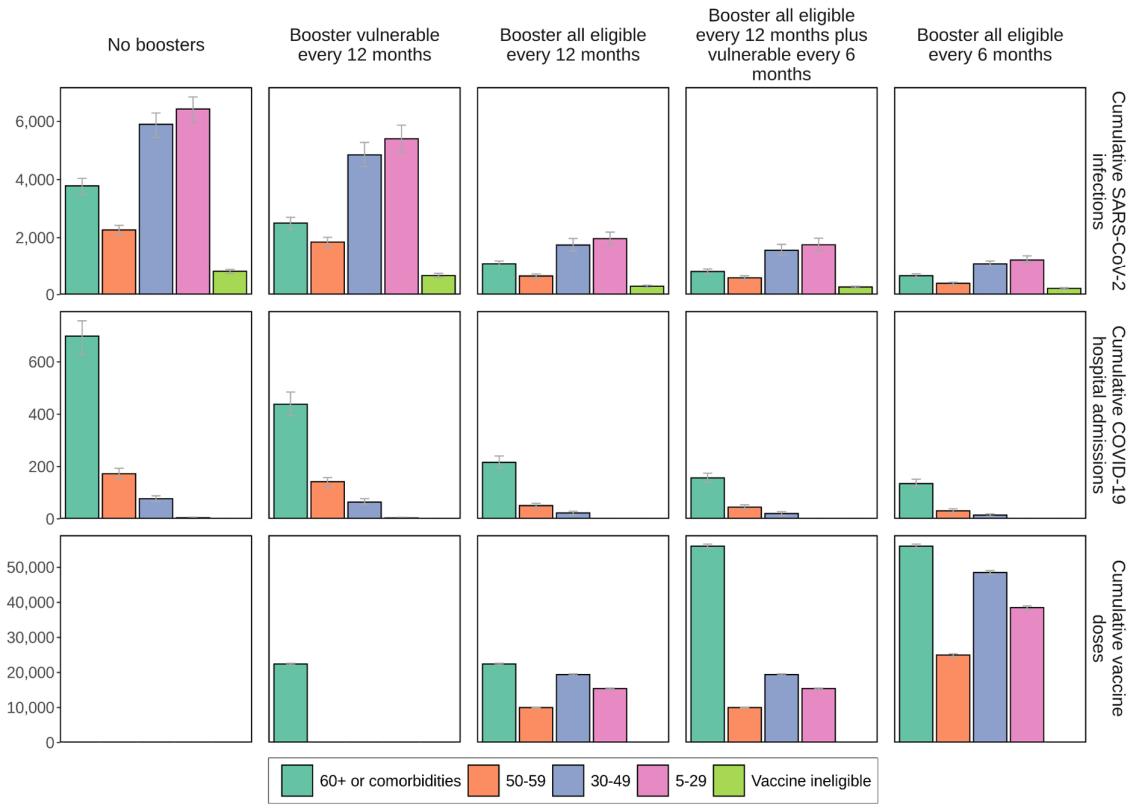

Figure S9: The cumulative projected impact of administering COVID-19 vaccine boosters to those most vulnerable or those eligible every twelve or six months. on SARS-CoV-2 infections and COVID-19-related hospital admissions by age and risk group over a two-year period in a simulated population of 100,000 individuals when new SARS-CoV-2 variants with 25% more infectiousness than the previously dominant variant but with the same severity as the Omicron variant emerged annually. Cumulative numbers of vaccine doses are shown in the bottom row. Error bars represent the stochastic uncertainty in model projections.

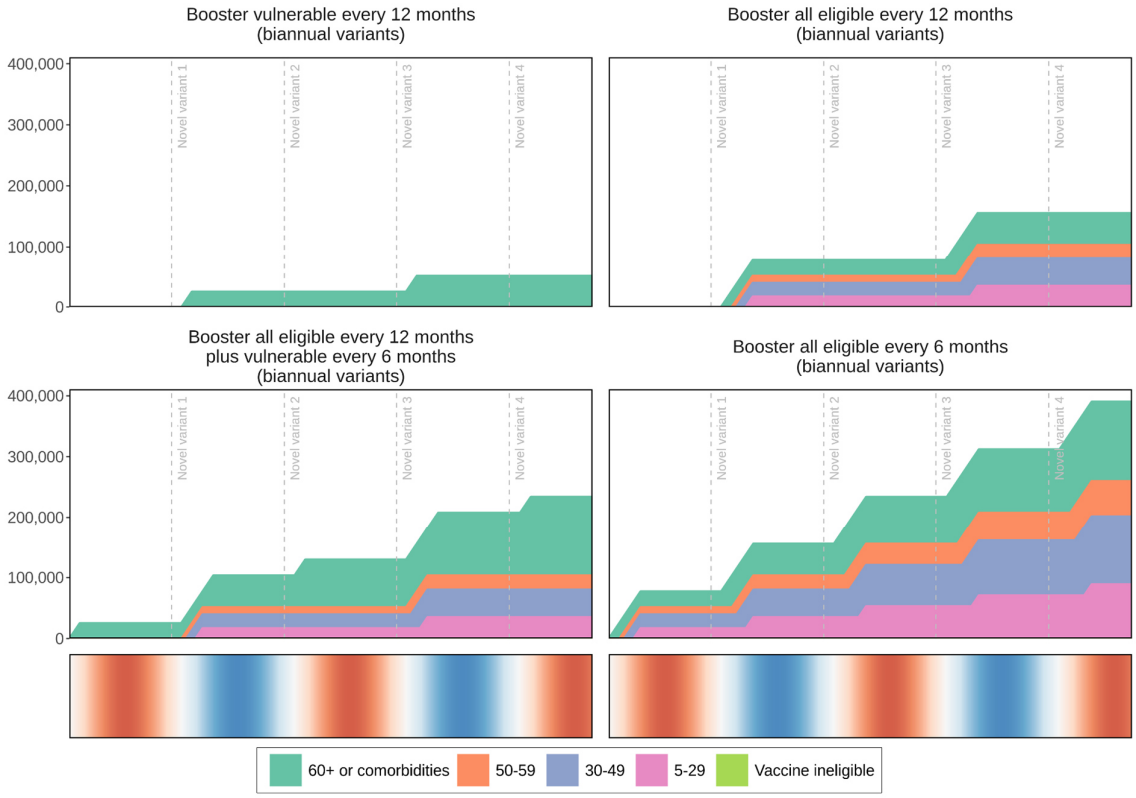

Figure S10: Cumulative COVID-19 vaccine booster dose administered by age and risk group for just over a two-year period in a simulated population of 100,000 individuals with those who previously received vaccine doses one and two are eligible to receive first-generation COVID-19 vaccine booster doses every twelve or six months. Those ineligible do not receive vaccine boosters (legend label corresponding to the light green shading). Boosting those most vulnerable every six months includes boosting all those eligible every twelve months (bottom row, left panel). Booster coverage was 98% of those who were eligible (universal coverage). Initial emergence indicated with horizontal dashed lines indicating where novel SARS-CoV-2 variants with a 25% more infectious and immune evading profile than the previously emerging variant were simulated to emerge every six months (the initial emergence of novel variants is indicated with horizontal dashed lines). Seasonality is illustrated in the bottom row where red shading indicates the warmer spring and summer seasons, blue the cooler fall and winter seasons, and white the seasonal transition periods.

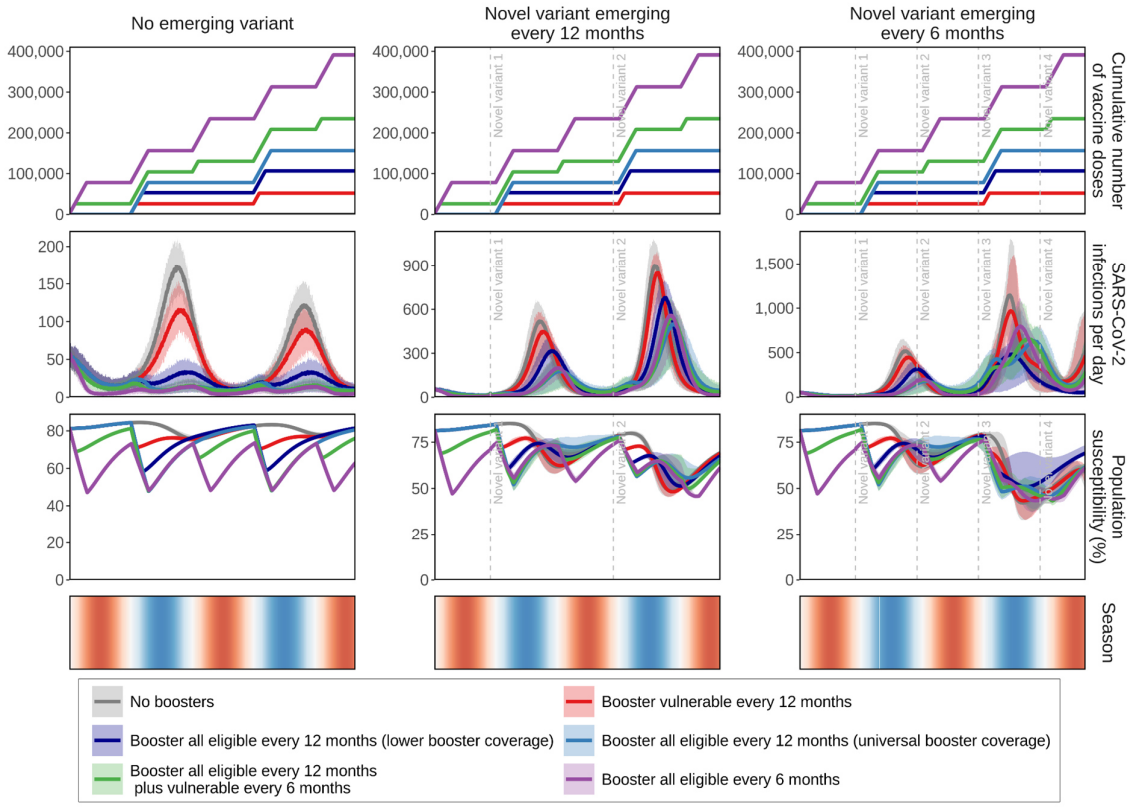

Figure S11: The cumulative number and timing of vaccine doses by scenario (top row, as shown in Figure 2 of the main text), projected daily impact of the various scenarios on SARS-CoV-2 infections (second row, corresponding to left panels from Figures S3B, S4B, and S5B), and daily percentage of population susceptibility by scenario (third row), in a simulated population of 100,000 individuals over a two-year period. People who previously received vaccine doses one and two are eligible to receive first-generation COVID-19 vaccine boosters. Those eligible received boosters every twelve or six months were aggregated into two groups, (1) those most vulnerable (60 years and older or persons with comorbidities) and (2) all eligible (five years and older). Boosting those most vulnerable every six months includes boosting all eligible people every twelve months. Grey curves represent the baseline scenario with no boosters modelled. Lower booster coverage (dark blue curve) was simulated as 85% coverage of those eligible 50 years of age and older and with comorbidities, and 50% of those eligible aged 5−49. Universal coverage (light blue curve) is 98% of those eligible to receive boosters. Scenarios were simulated as having (i) no novel emerging SARS-CoV-2 variant, assuming the same infectiousness and severity of the Omicron variant (left panels), (ii) novel variants with 25% more infectiousness and immune evading capacity emerging every twelve months (center panels), or (iii) emerging every six months (right panels) (initial emergence indicated with horizontal dashed lines). Shaded areas represent the stochastic uncertainty surrounding projections. Seasonality is illustrated in the bottom row where red shading indicates the warmer spring and summer seasons, blue the cooler fall and winter seasons, and white the seasonal transition periods.

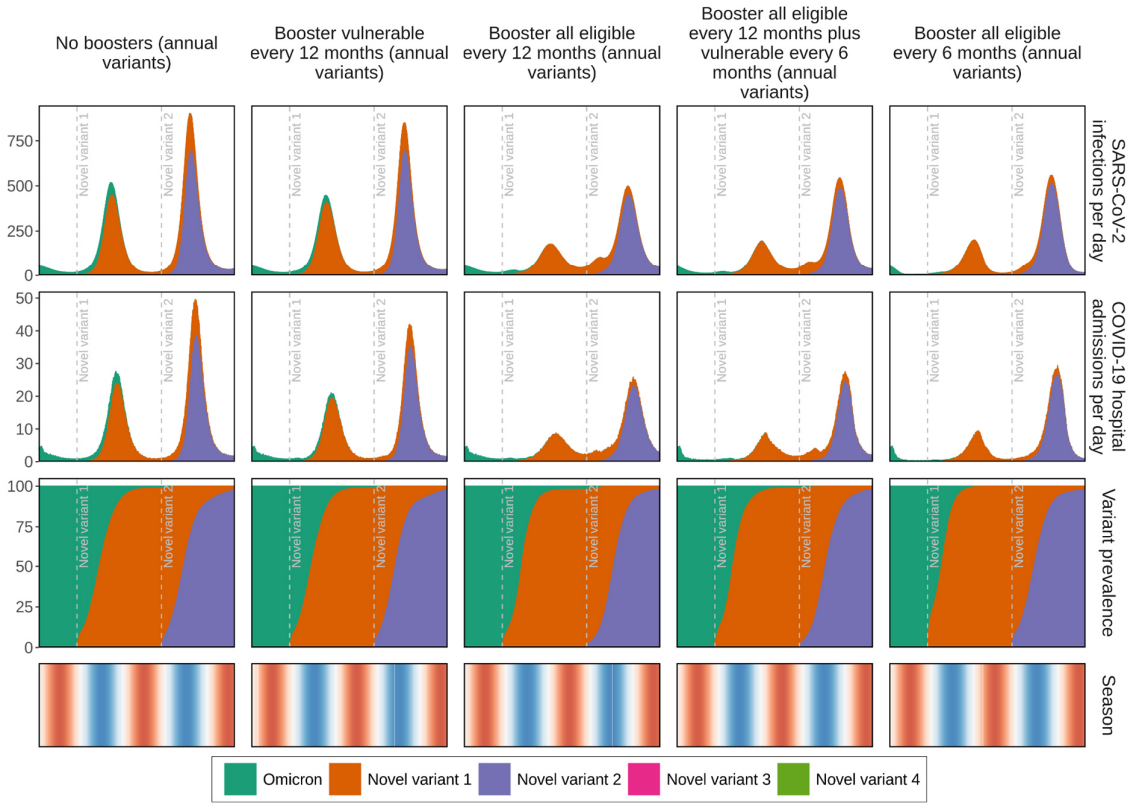

Figure S12A: Projected impact of COVID-19 vaccine boosters on new daily SARS-CoV-2 infections and COVID-19-related hospital admissions by novel SARS-CoV-2 variant (stacked shaded areas under the curves) for just over a two-year period in a simulated population of 100,000 individuals. Those who previously received vaccine doses one and two were eligible to receive first-generation COVID-19 vaccine boosters. Populations who received boosters every twelve or six months are aggregated into two groups, (1) those most vulnerable (60 years and older or persons with comorbidities) and (2) all eligible (five years and older). Universal coverage of booster doses is 98% of those eligible. Novel variants with 25% more infectiousness and immune evading capacity but with the same severity as the Omicron variant emerged annually (initial emergence indicated with horizontal dashed lines, legend labels for novel variant 3 (pink) and novel variant 4 (lime green) do not apply in this figure). Prevalence by variant is plotted in the third row. Seasonality is illustrated in the bottom row where red shading indicates the warmer spring and summer seasons, blue the cooler fall and winter seasons, and white the seasonal transition periods.

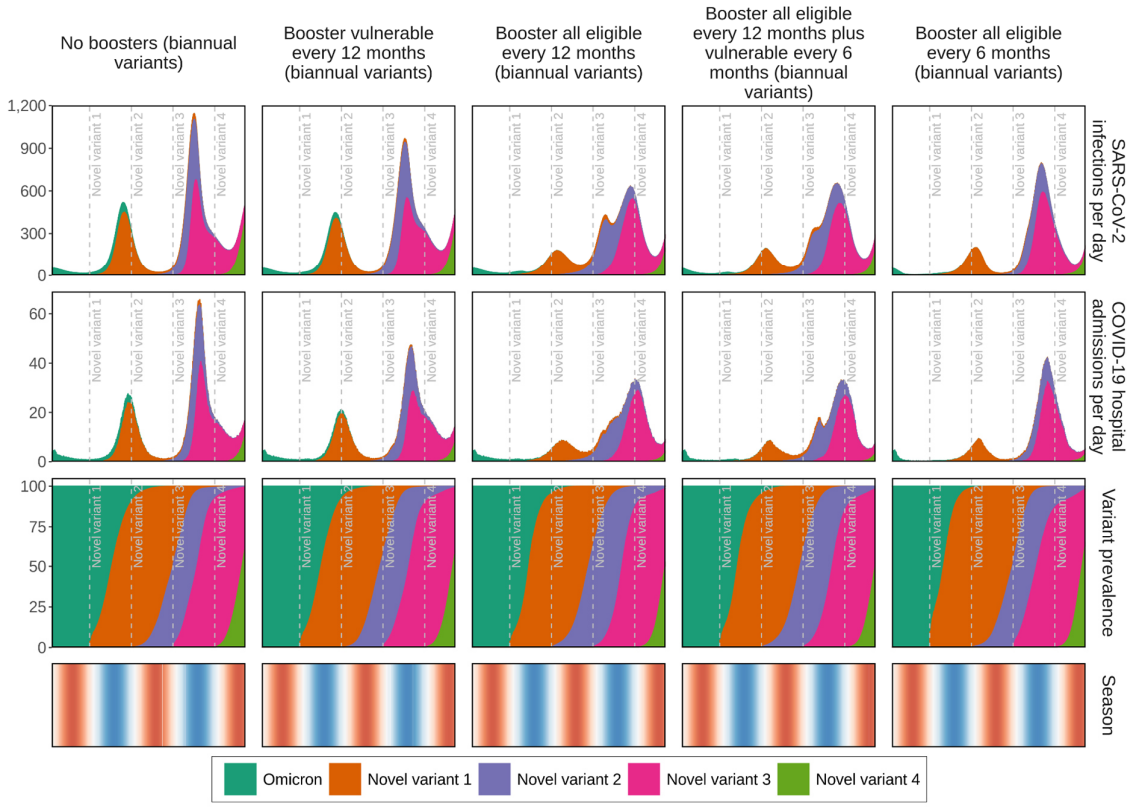

Figure S12B: Projected impact of COVID-19 vaccine boosters on new daily SARS-CoV-2 infections and COVID-19-related hospital admissions by novel SARS-CoV-2 variant (stacked shaded areas under the curves) for just over a two-year period in a simulated population of 100,000 individuals. Those who previously received vaccine doses one and two were eligible to receive first-generation COVID-19 vaccine boosters. Populations who received boosters every twelve or six months are aggregated into two groups, (1) those most vulnerable (60 years and older or persons with comorbidities) and (2) all eligible (five years and older). Universal coverage of booster doses is 98% of those eligible. Novel variants with 25% more infectiousness and immune evading capacity emerged every six months (initial emergence indicated with initial emergence indicated with horizontal dashed lines). Prevalence by variant is plotted in the third row. Seasonality is illustrated in the bottom row where red shading indicates the warmer spring and summer seasons, blue the cooler fall and winter seasons, and white the seasonal transition periods.

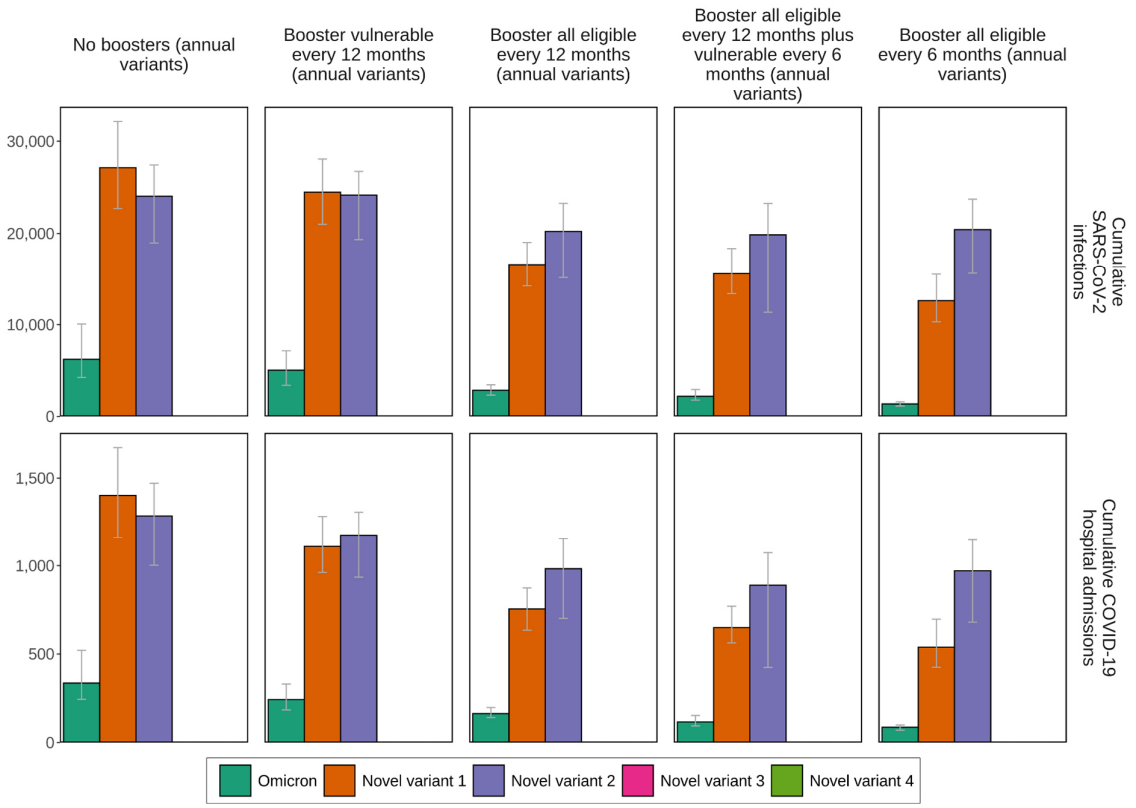

Figure S13A: Cumulative projected impact of COVID-19 vaccine boosters on SARS-CoV-2 infections and COVID-19-related hospital admissions by variant when new SARS-CoV-2 variants with 25% more infectiousness and immune evading capacity but with the same severity as the Omicron variant emerged annually (legend labels for novel variant 3 (pink) and novel variant 4 (lime green) do not apply in this figure). This was simulated for just over a two-year period in a population of 100,000 individuals. Those who previously received vaccine doses one and two were eligible to receive first-generation COVID-19 vaccine boosters. Populations who received boosters every twelve or six months are aggregated into two main groups, (1) those most vulnerable (60 years and older or persons with comorbidities), and (2) all eligible (five years and older). Boosting those most vulnerable every six months includes boosting all those eligible every twelve months. Universal booster coverage represents 98% of those eligible received booster doses. Error bars shown represent the stochastic uncertainty in model projections.

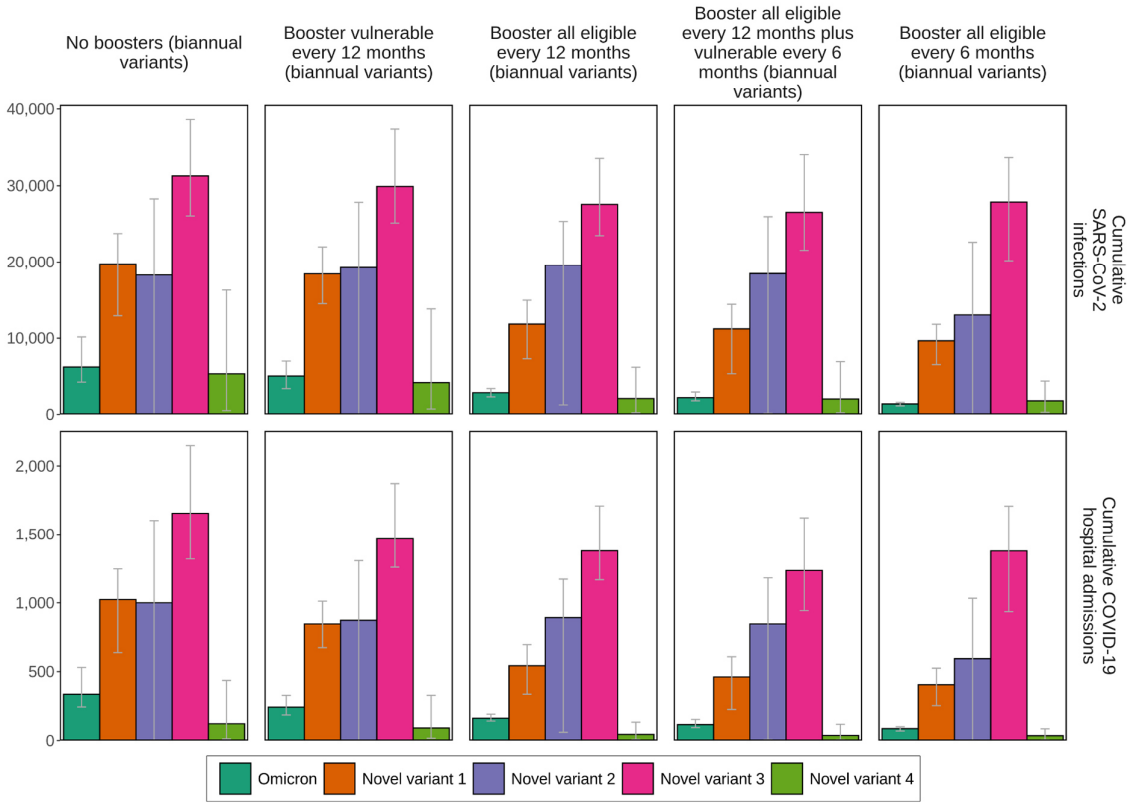

Figure S13B: Cumulative projected impact of COVID-19 vaccine boosters on SARS-CoV-2 infections and COVID-19-related hospital admissions by variant when novel SARS-CoV-2 variants with 25% more infectiousness and immune evading capacity emerged every six months. This was simulated for just over a two-year period in a population of 100,000 individuals. Those who previously received vaccine doses one and two were eligible to receive first-generation COVID-19 vaccine boosters. Populations who received boosters every twelve or six months are aggregated into two main groups, (1) those most vulnerable (60 years and older or persons with comorbidities), and (2) all eligible (five years and older). Boosting those most vulnerable every six months includes boosting all those eligible every twelve months. Universal booster coverage represents 98% of those eligible received booster doses. Error bars shown represent the stochastic uncertainty in model projections. Novel variant four only emerges at the end of the simulation period; therefore, its full impact is not yet captured.

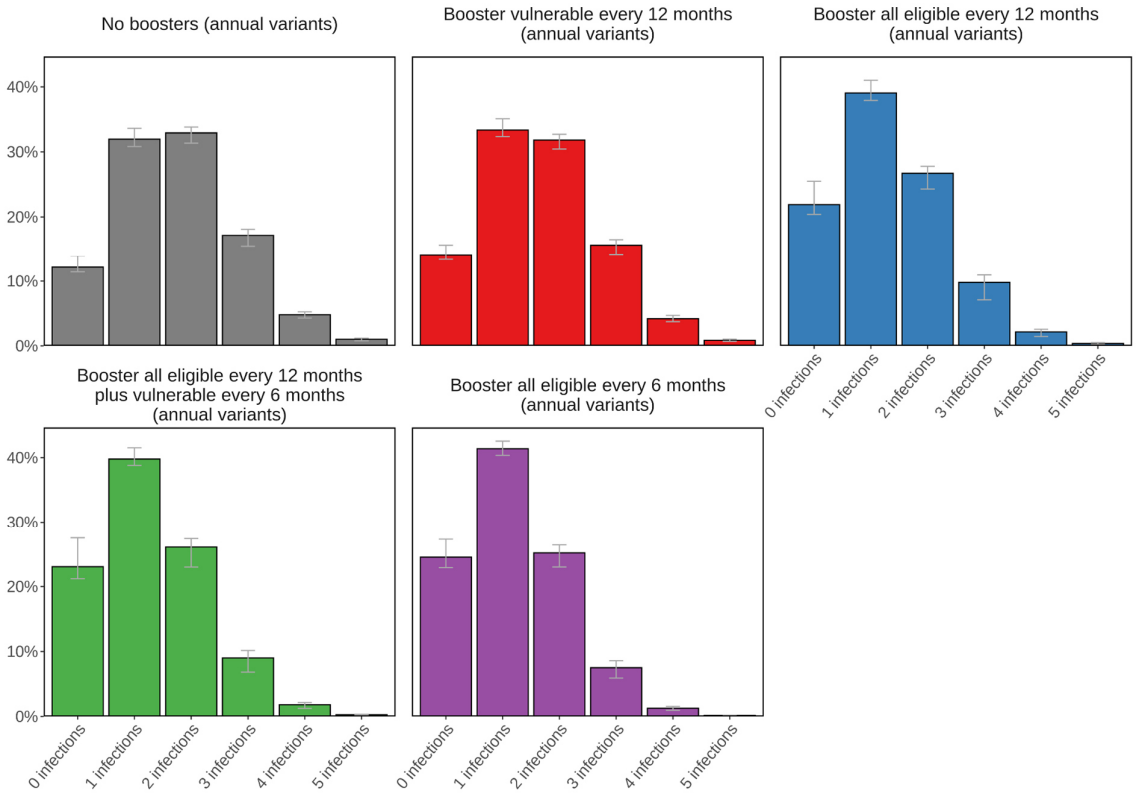

Figure S14A: Cumulative projected impact of COVID-19 vaccine boosters on the percentage of SARS-CoV-2 infections (and re-infections) when novel SARS-CoV-2 variants with 25% more infectiousness and immune evading capacity emerged annually. This was simulated for just over a two-year period in a population of 100,000 individuals. Those who previously received vaccine doses one and two were eligible to receive first-generation COVID-19 vaccine boosters. Populations who received boosters every twelve or six months are aggregated into two main groups, (1) those most vulnerable (60 years and older or persons with comorbidities), and all eligible (five years and older). Boosting those most vulnerable every six months includes boosting all those eligible every twelve months. Grey bars represent infections from the baseline scenario with no vaccine boosters. Universal booster coverage represents 98% of those eligible received booster doses. Error bars shown represent the stochastic uncertainty in model projections.

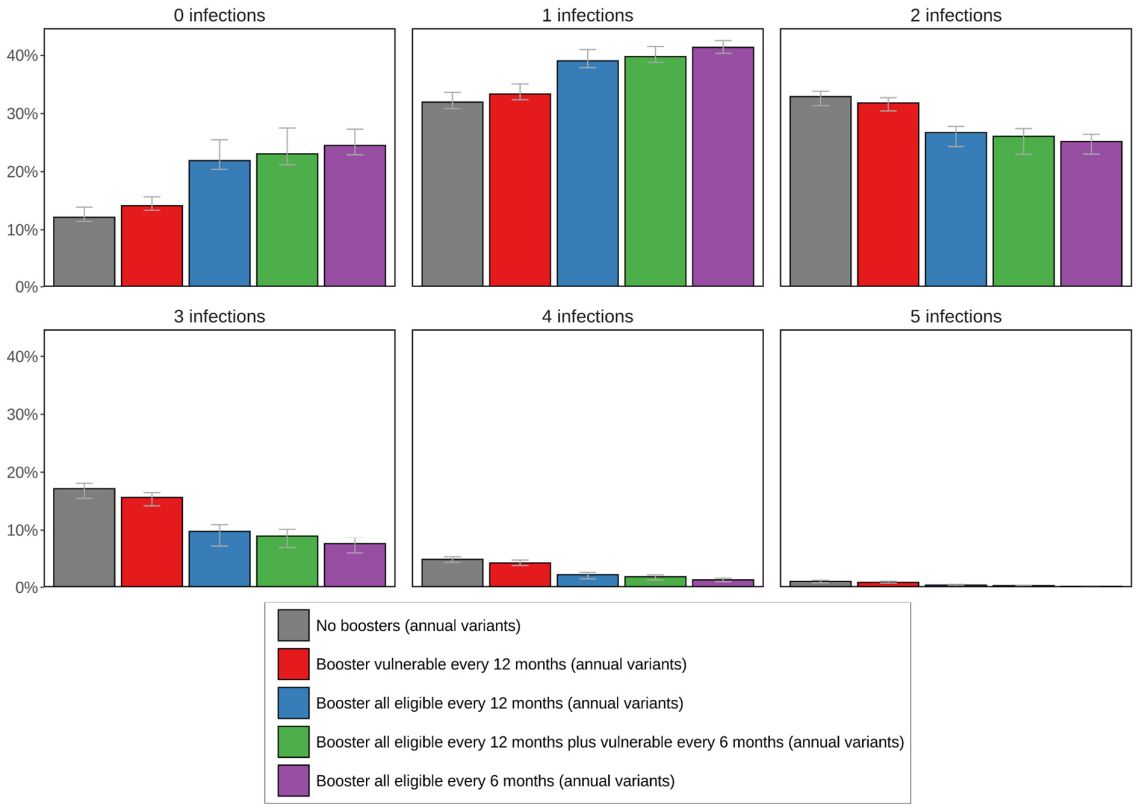

Figure S14B: Cumulative projected impact of COVID-19 vaccine boosters on the percentage of SARS-CoV-2 infections (and re-infections) grouped by number of infections when novel SARS-CoV-2 variants with 25% more infectiousness and immune evading capacity emerged annually. This was simulated for just over a two-year period in a population of 100,000 individuals. Those who previously received vaccine doses one and two were eligible to receive first-generation COVID-19 vaccine boosters. Populations who received boosters every twelve or six months are aggregated into two main groups, (1) those most vulnerable (60 years and older or persons with comorbidities), and (2) all eligible (five years and older). Boosting those most vulnerable every six months includes boosting all those eligible every twelve months. Grey bars represent infections from the baseline scenario with no vaccine boosters. Universal booster coverage represents 98% of those eligible received booster doses. Error bars shown represent the stochastic uncertainty in model projections.

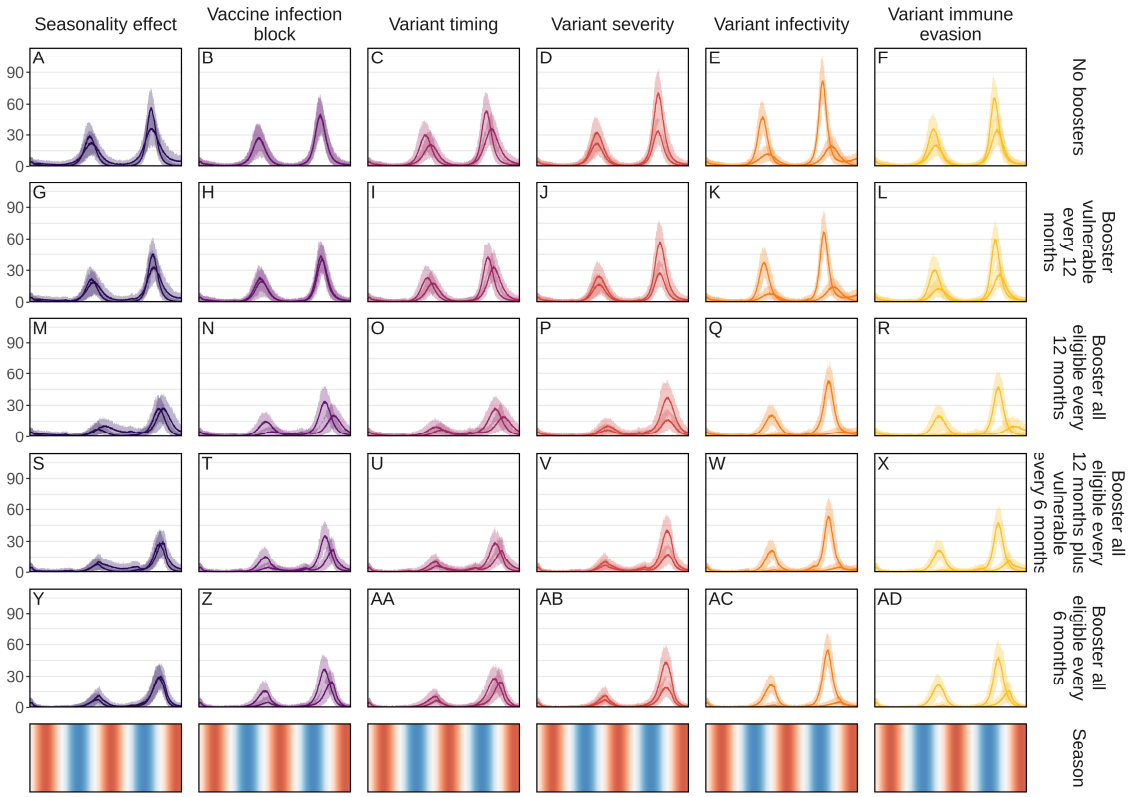

Figure S15: Sensitivity analysis showing the projected impact on COVID-19-related hospital admissions averted over a two-year period from modifying seasonality effect, vaccine infection blocking, variant timing, variant severity, variant infectivity, and variant immune evasion with the two curves in each panel representing the lower and upper bound values for each parameter as listed in Table 1 of the main text. This time series was simulated for just over a two-year period in a population of 100,000 individuals. Those who previously received vaccine doses one and two were eligible to receive first-generation COVID-19 vaccine boosters. Populations who received boosters every twelve or six months are aggregated into two main groups, (1) those most vulnerable (60 years and older or persons with comorbidities), and (2) all eligible (five years and older). Boosting those most vulnerable every six months includes boosting all those eligible every twelve months. No boosters (top row) represents the baseline scenario with no vaccine boosters administered. Seasonality is illustrated in the bottom row where red shading indicates the warmer spring and summer seasons, blue the cooler fall and winter seasons, and white the seasonal transition periods.

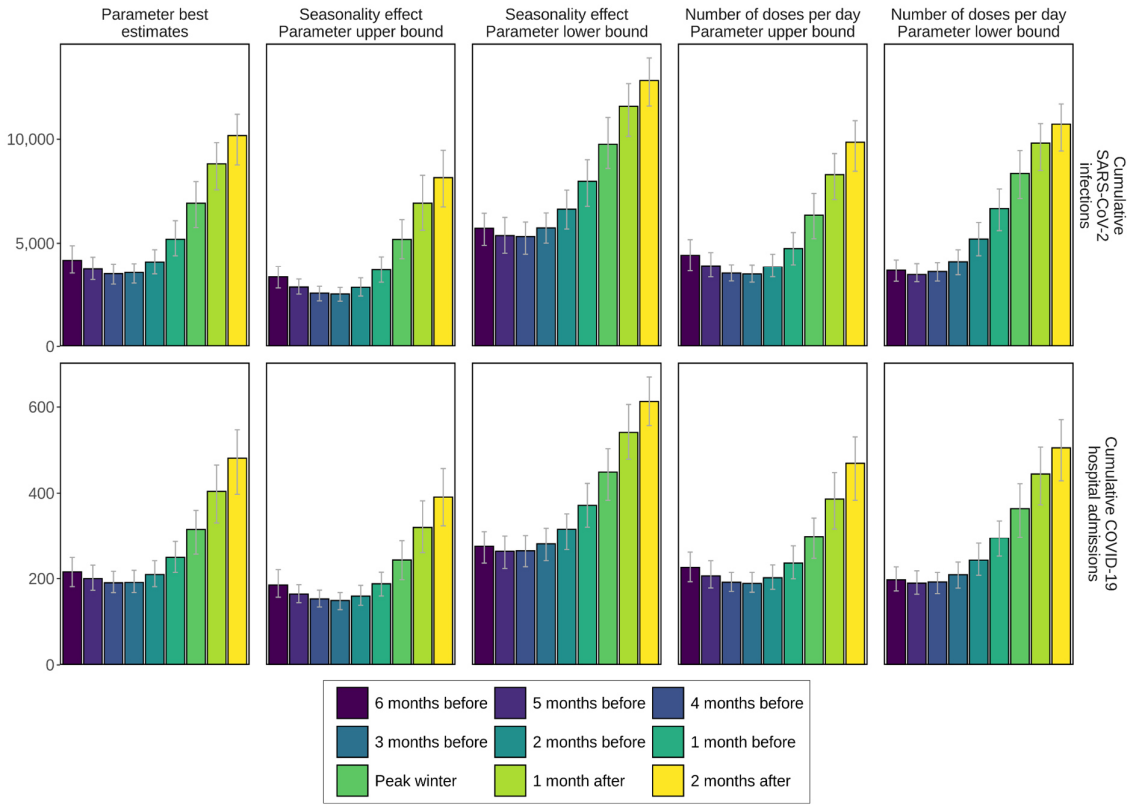

Figure S16A: Impact of varying vaccine booster dose timing from six months before to two month after peak winter on the cumulative SARS-CoV-2 infections and COVID-19-related hospital admissions over a two-year period.

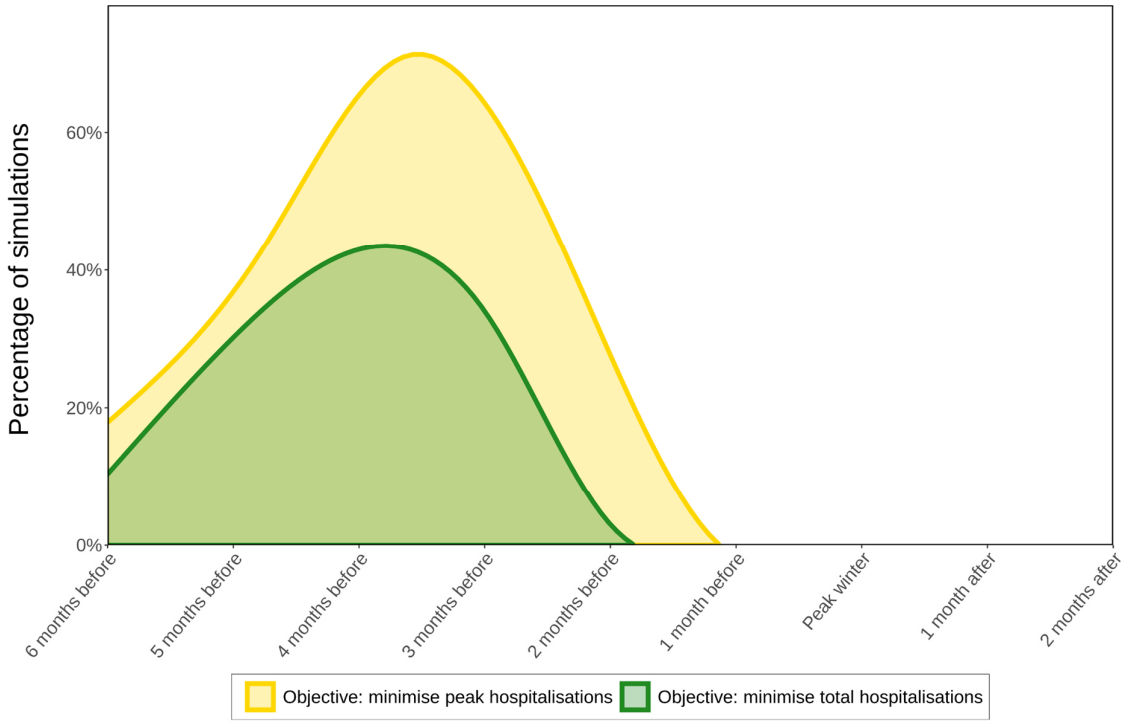

Figure S16B: Percentage of simulations to optimise the start of COVID-19 vaccine booster roll-out considering parameter and stochastic uncertainty to either minimise peak hospitalisations (yellow area curve) or total hospitalisations (green area curve) from six months before to two months after peak winter.

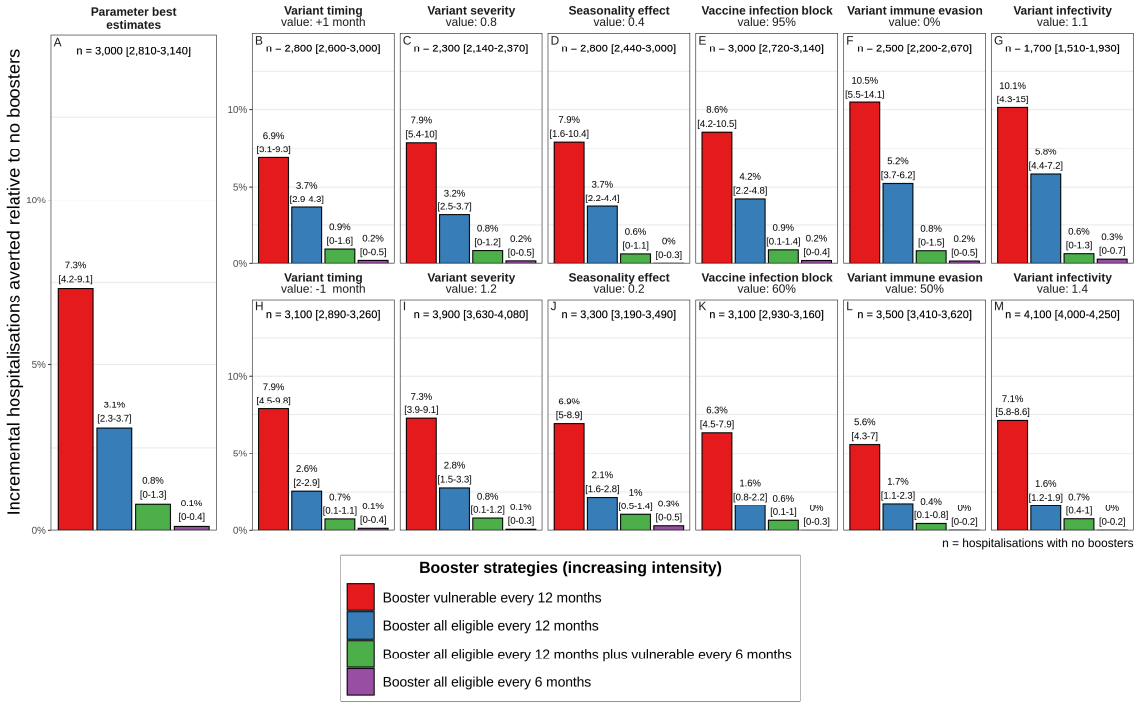

Figure S17: Percentage of COVID-19-related hospitalisations averted over a two-year period per 100,000 COVID-19 vaccine booster doses administered relative to no boosters given to those who received the first two doses and are most vulnerable (60 years and older or persons with comorbidities) or all eligible (five years and older) every twelve or six months, alongside varying the variant timing, variant severity, seasonality, vaccine infection blocking, variant immune evasion, and variant infectivity from best estimate values as listed in Table 1. Uncertainty bounds are shown in brackets above each bar. The numbers of hospitalisations with no boosters (n) with uncertainty bounds are shown at the top of each panel.

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