Supplemental Tables and Figures

Table S1: Number of non-severe COVID-19 cases, risk, and number needed to treat to avert non-severe COVID-19 in six risk groups with different frequencies of COVID-19 booster vaccination.
Table S2: Number of severe COVID-19 cases, risk, and number needed to treat to avert severe COVID-19 in four age groups among the mild immunocompromised population with different frequencies of COVID-19 booster vaccination.
Table S3: Number of severe COVID-19 cases, risk, and number needed to treat to avert severe COVID-19 in four age groups among the moderate/severe immunocompromised population with different frequencies of COVID-19 booster vaccination.
Table S4: Number of severe COVID-19 cases and risk in six risk groups with no additional COVID-19 booster vaccination.
Table S5: Sensitivity analysis of pessimistic waning on the number of severe COVID-19 cases, risk, and number needed to treat to avert severe COVID-19 in six risk groups with different frequencies of COVID-19 booster vaccination.
Table S6: Sensitivity analysis of optimistic waning on the number of severe COVID-19 cases, risk, and number needed to treat to avert severe COVID-19 in six risk groups with different frequencies of COVID-19 booster vaccination.
Table S7: Sensitivity analysis of pessimistic vaccine effectiveness on the number of severe COVID-19 cases, risk, and number needed to treat to avert severe COVID-19 in six risk groups with different frequencies of COVID-19 booster vaccination.
Table S8: Sensitivity analysis of optimistic vaccine effectiveness on the number of severe COVID-19 cases, risk, and number needed to treat to avert severe COVID-19 in six risk groups with different frequencies of COVID-19 booster vaccination.
Table S9: Sensitivity analysis of higher severe COVID-19 incidence on the number of severe COVID-19 cases, risk, and number needed to treat to avert severe COVID-19 in six risk groups with different frequencies of COVID-19 booster vaccination.
Table S10: Sensitivity analysis of lower severe COVID-19 incidence on the number of severe COVID-19 cases, risk, and number needed to treat to avert severe COVID-19 in six risk groups with different frequencies of COVID-19 booster vaccination.
Table S11: Sensitivity analysis of lower seroprevalence on the number of severe COVID-19 cases, risk, and number needed to treat to avert severe COVID-19 in six risk groups with different frequencies of COVID-19 booster vaccination.
Table S12: Sensitivity analysis of higher seroprevalence on the number of severe COVID-19 cases, risk, and number needed to treat to avert severe COVID-19 in six risk groups with different frequencies of COVID-19 booster vaccination.
Table S13: Sensitivity analysis of 100% seroprevalence on the number of severe COVID-19 cases, risk, and number needed to treat to avert severe COVID-19 in six risk groups with different frequencies of COVID-19 booster vaccination.
Table S14: Sensitivity analysis of five-year simulation period on the number of severe COVID-19 cases, risk, and number needed to treat to avert severe COVID-19 in six risk groups with different frequencies of COVID-19 booster vaccination.
Table S15: Sensitivity analysis of delayed vaccination administration on the number of severe COVID-19 cases, risk, and number needed to treat to avert severe COVID-19 in six risk groups with different frequencies of COVID-19 booster vaccination.

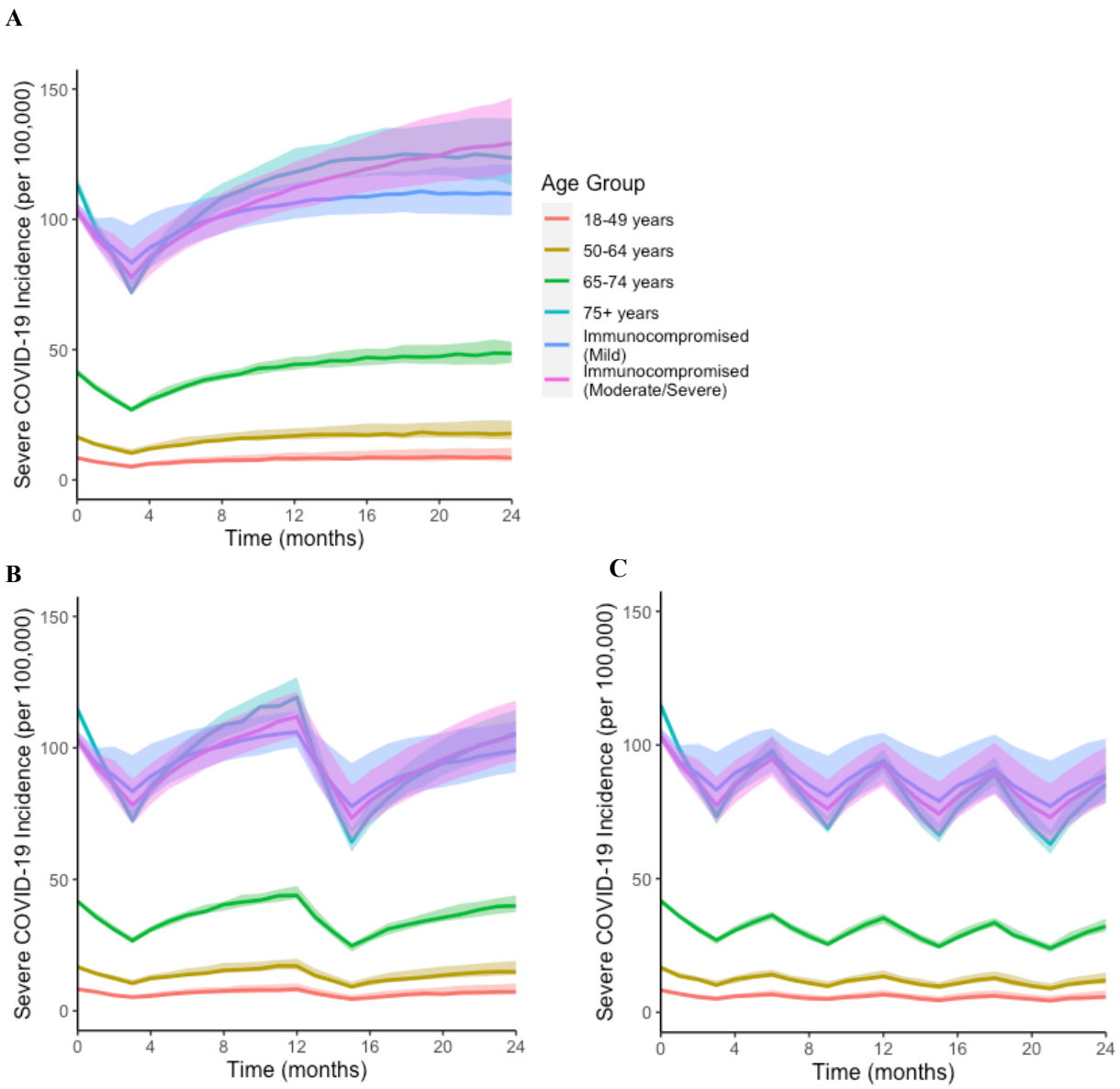


Figure S1: Monthly incidence of severe COVID-19 in four age groups and two immunocompromised groups over a two-year simulation period with different frequencies of COVID-19 booster vaccination. We simulated three COVID-19 booster vaccine schedules with the mRNA dose: (A) One-time booster (total of 1 dose); (B) annual booster (total of 2 doses); (C) booster every 6 months (total of 4 doses). We estimated incidence of severe COVID-19 per 100,000 persons (y-axis) over time in months (x-axis), by age group and immunocompromised population in Panels A-C. We modeled the protection of a booster (administered in the population over a 3-month period) to restore vaccine-induced protection that waned over time based on published literature, which reduced severe COVID-19 cases. More frequent booster vaccination (panel B-C) reduced total severe COVID-19 cases compared to one-time booster (panel A), and this benefit was most pronounced in the oldest age groups. The uncertainty intervals are based on 95% CI of published literature of waning data, in addition to uncertainty in baseline seroprevalence and non-severe infection multiplier estimates.

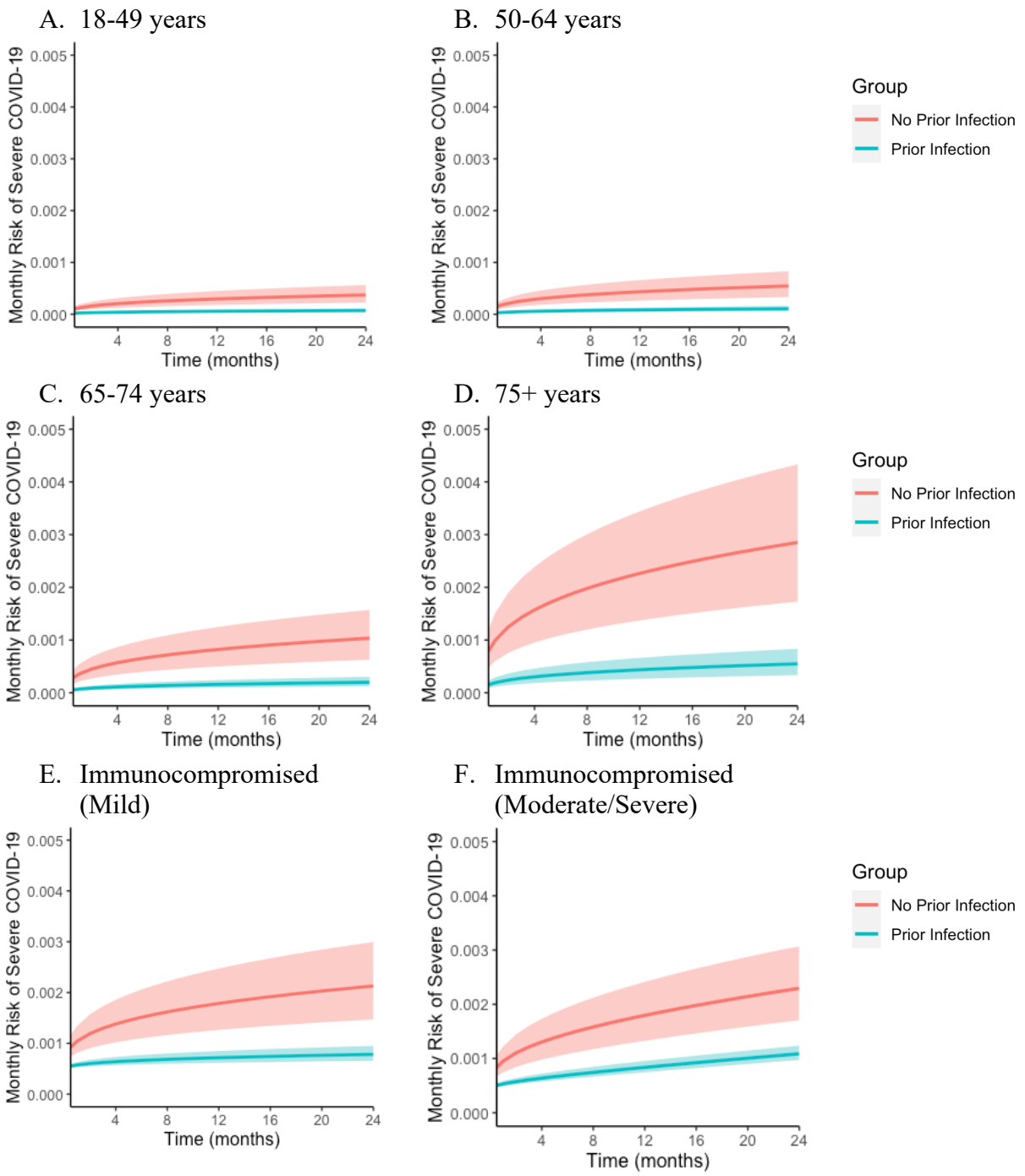
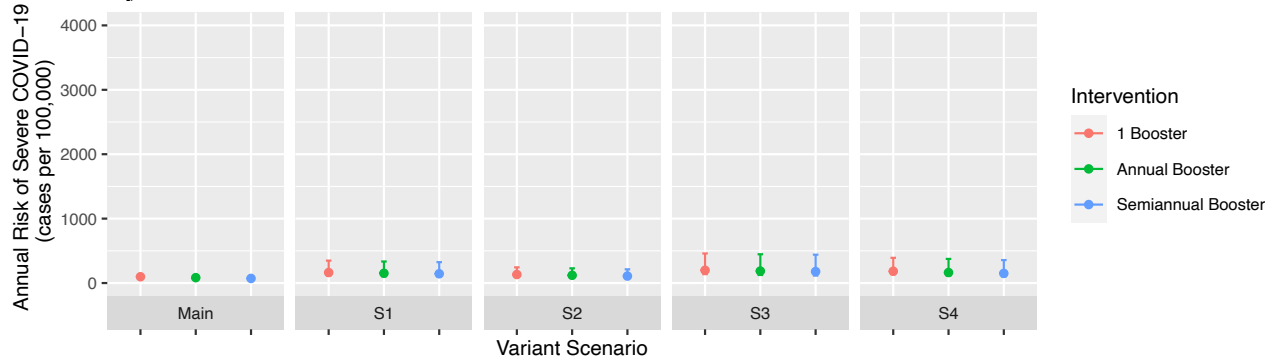
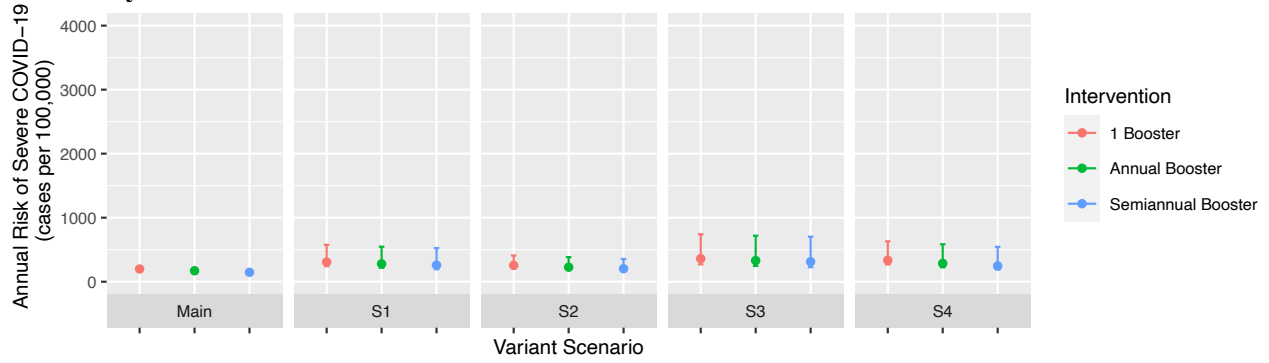


Figure S2: Risk of severe COVID-19 over time by baseline risk and waning protection. We modeled risk of severe COVID-19 by baseline risk and time since last immune event (vaccine or infection) by multiplying age-specific lambdas to protection estimates over time. The risk groups modeled here are the (A) 18-49 years; (B) 50-64 years; (C) 65-74 years; (D) 75+ years; (E) Immunocompromised (mild); and (F) Immunocompromised (moderate/severe).

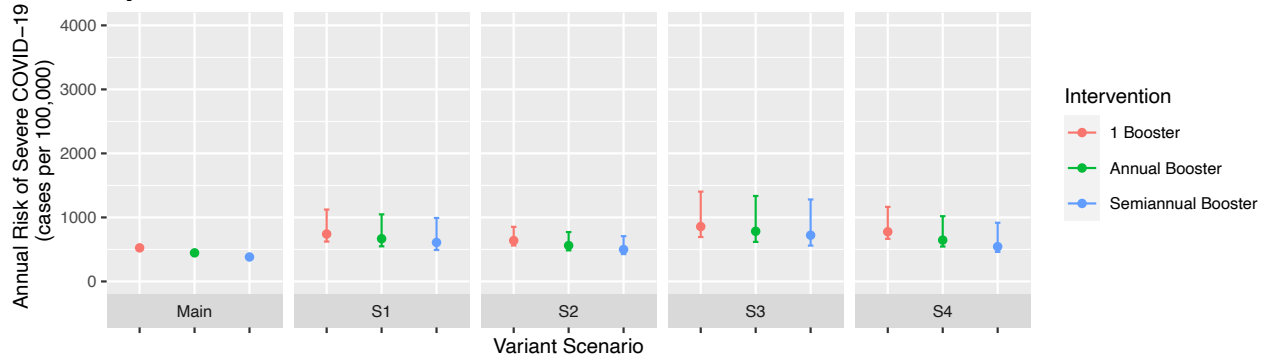
A. 18-49 years



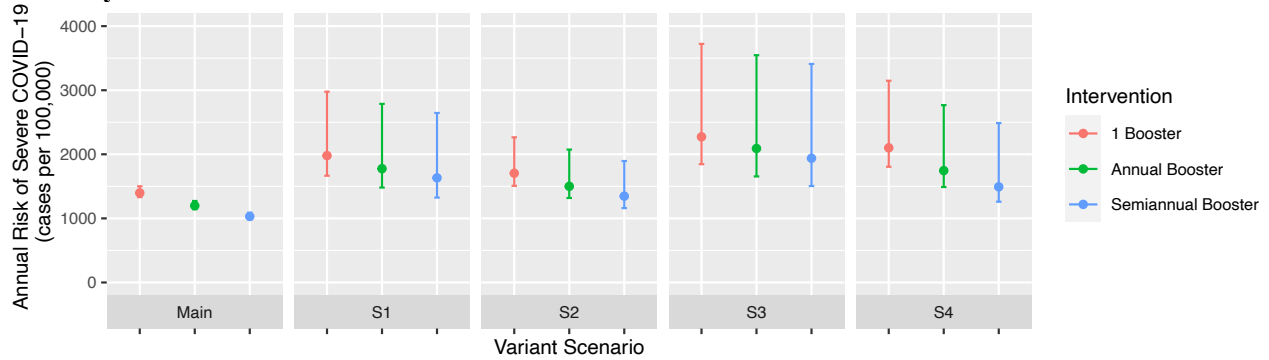
B. 50-64 years



C. 65-74 years



D. 75+ years



E. Immunocompromised (Mild)

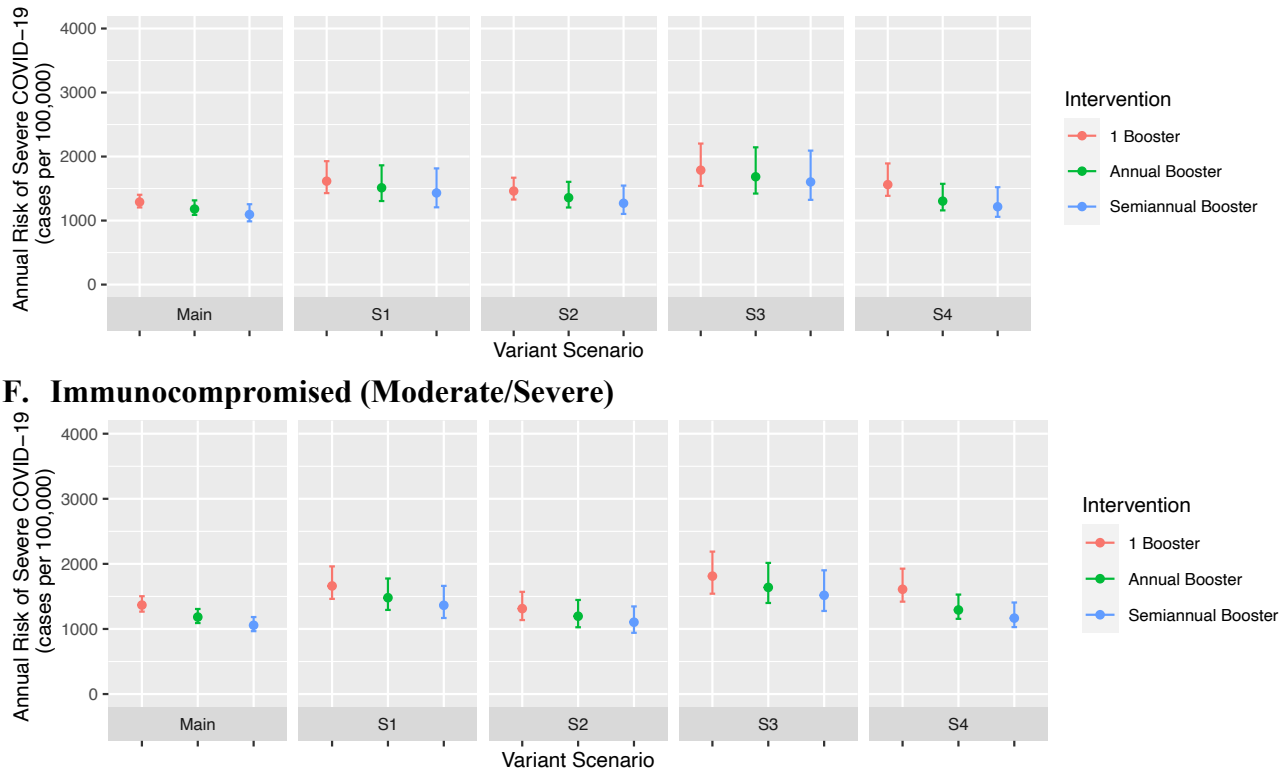
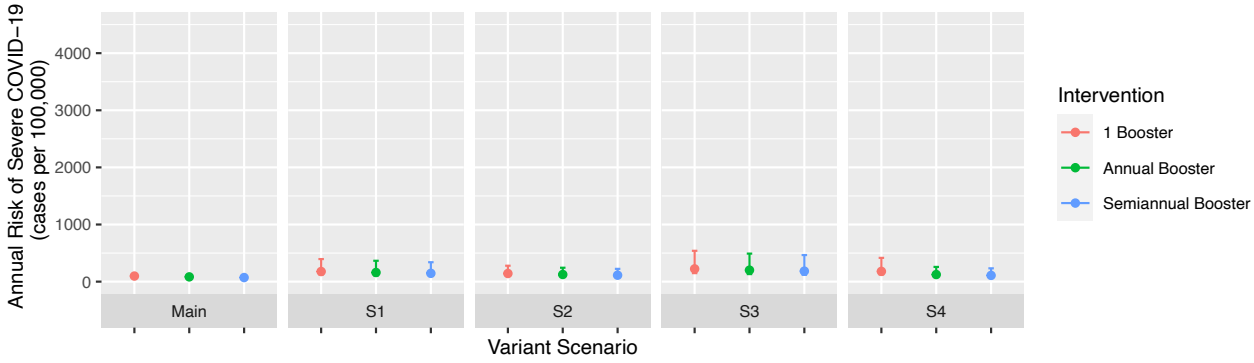
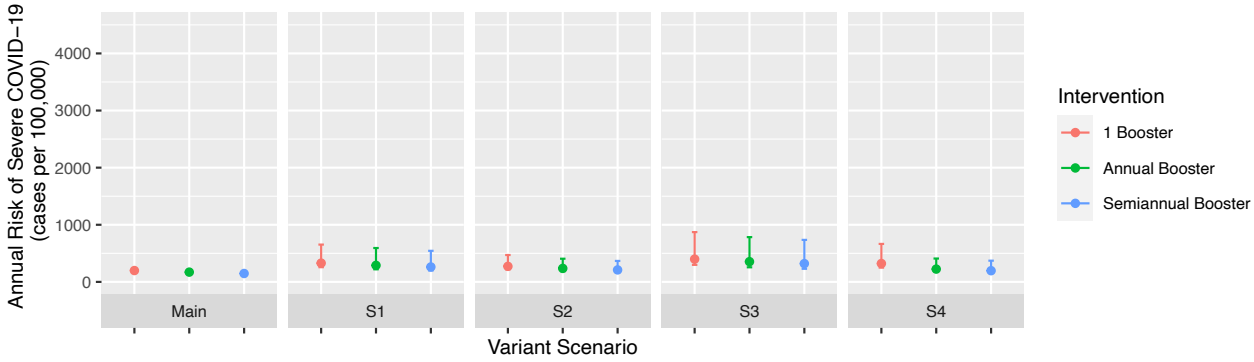


Figure S3: Scenario analysis on emergence of novel SARS-CoV-2 variants with immune evasion (10% reduction in immunity) comparing severe COVID-19 risk with different frequencies of COVID-19 booster vaccination. We simulated four scenarios on emergence of novel variant(s) with reduced susceptibility to protection generated by prior vaccination and natural infection. Under each variant scenario analysis, we simulated three frequencies of COVID-19 booster vaccine for four age groups and two immunocompromised groups. We plotted absolute annual risk of severe COVID-19 over a two-year simulation. The vertical bars represent uncertainty intervals, which simulate different scenarios of baseline conditions to account for uncertain model inputs. Intervals are designed to demonstrate uncertainty within a single vaccine strategy; comparison between vaccine strategies should be use the same assumed baseline conditions.

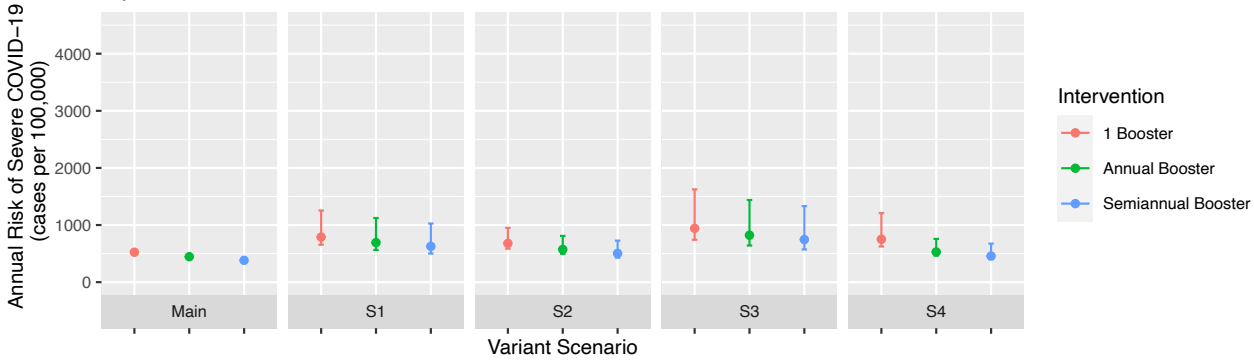
A. 18-49 years



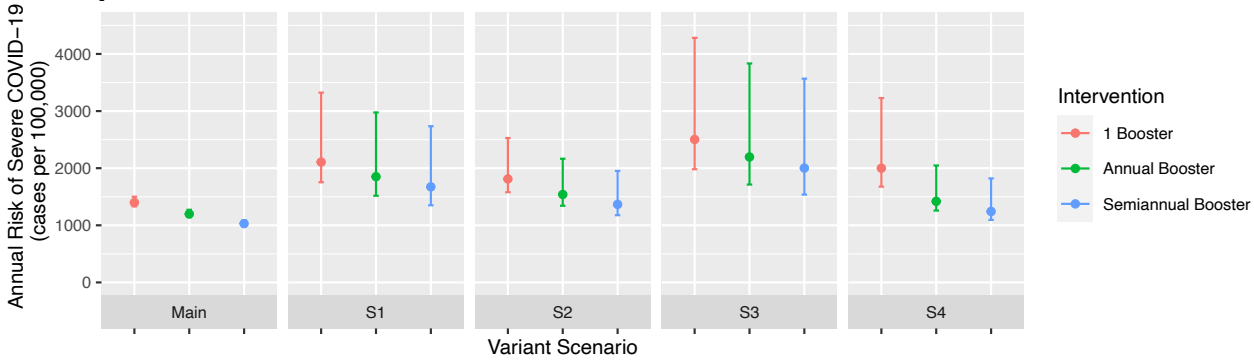
B. 50-64 years



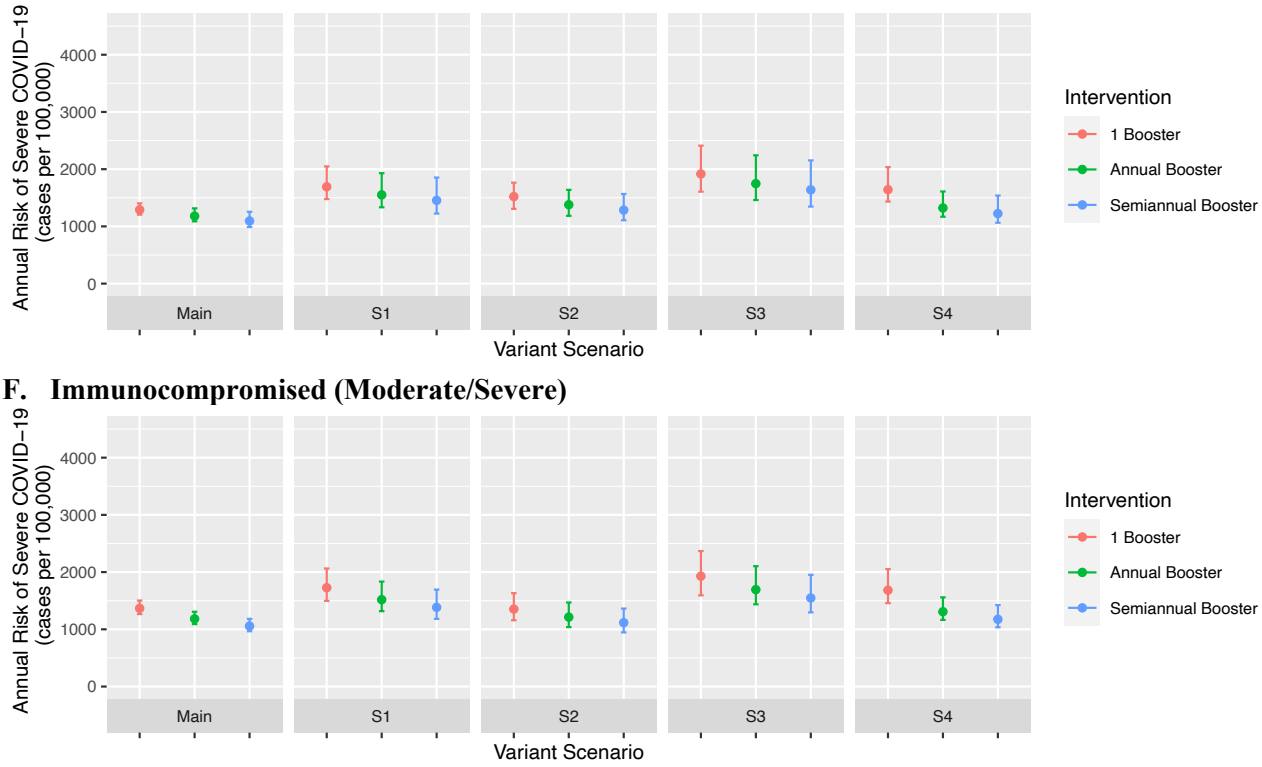
C. 65-74 years



D. 75+ years



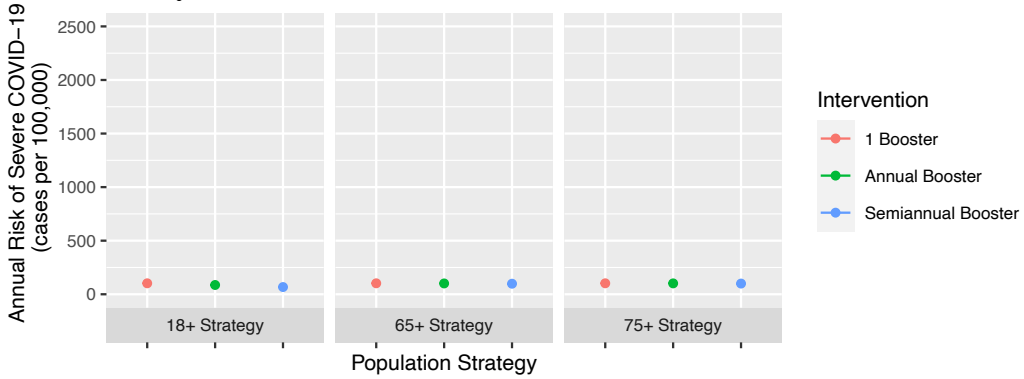
E. Immunocompromised (Mild)



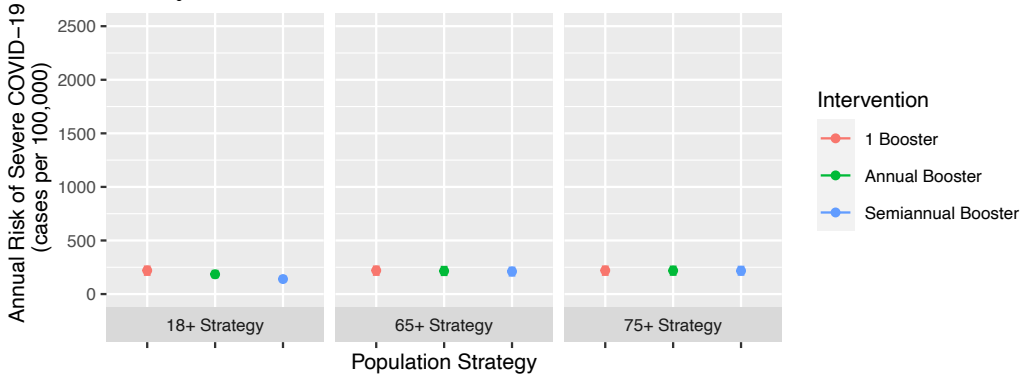
F. Immunocompromised (Moderate/Severe)

Figure S4: Scenario analysis on emergence of novel SARS-CoV-2 variants with immune evasion (10% absolute reduction and 5% increased rate of waning) comparing severe COVID-19 risk with different frequencies of COVID-19 booster vaccination. We simulated four scenarios on emergence of novel variant(s) with reduced susceptibility to protection generated by prior vaccination and natural infection. Under each variant scenario analysis, we simulated three frequencies of COVID-19 booster vaccine for four age groups and two immunocompromised groups. We plotted absolute annual risk of severe COVID-19 over a two-year simulation. The vertical bars represent uncertainty intervals, which simulate different scenarios of baseline conditions to account for uncertain model inputs. Intervals are designed to demonstrate uncertainty within a single vaccine strategy; comparison between vaccine strategies should be use the same assumed baseline conditions.

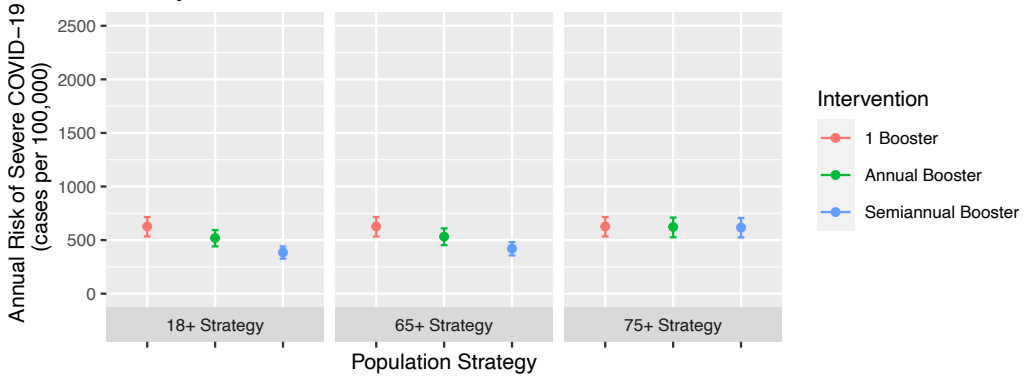
A. 18-49 years



B. 50-64 years



C. 65-74 years



D. 75+ years

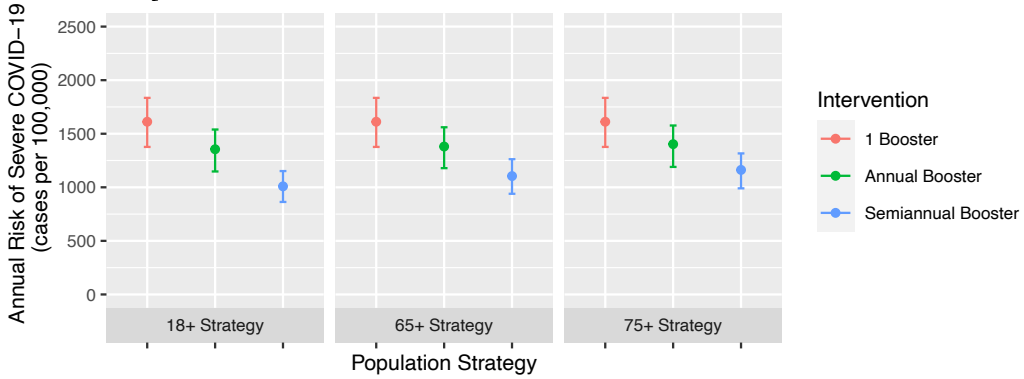
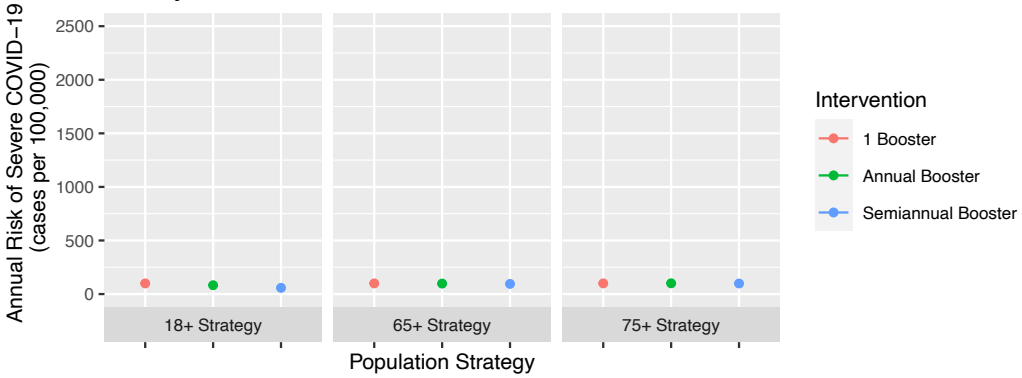
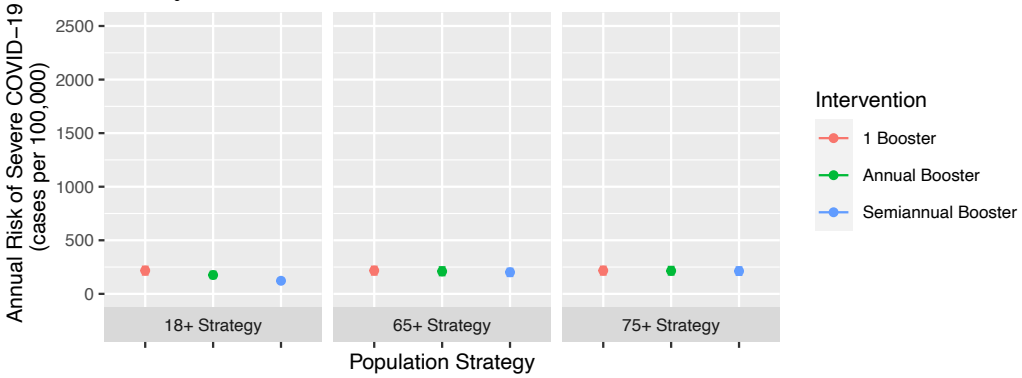


Figure S5: Scenario analysis using a dynamic transmission model under realistic coverage assumptions to estimate the impact of indirect effects on COVID-19 booster vaccination strategies in four age groups and two immunocompromised groups. We used a dynamic transmission model to compare different frequencies of COVID-19 booster vaccine in the following groups: (A) 75+ years, moderate/severe immunocompromised group; (B) 65+ years and all immunocompromised groups; and (C) 18+ years in all groups. We assumed a background of one-time booster vaccination at the start of the simulation in adults (18+ years) with age-specific coverage based on current uptake. We plotted absolute annual risk of severe COVID-19 over a two-year simulation in four age groups and two immunocompromised groups, to compare the indirect effects of booster vaccination on all risk groups. Table A7 reports the coverage estimates (realistic vaccine uptake assumption).

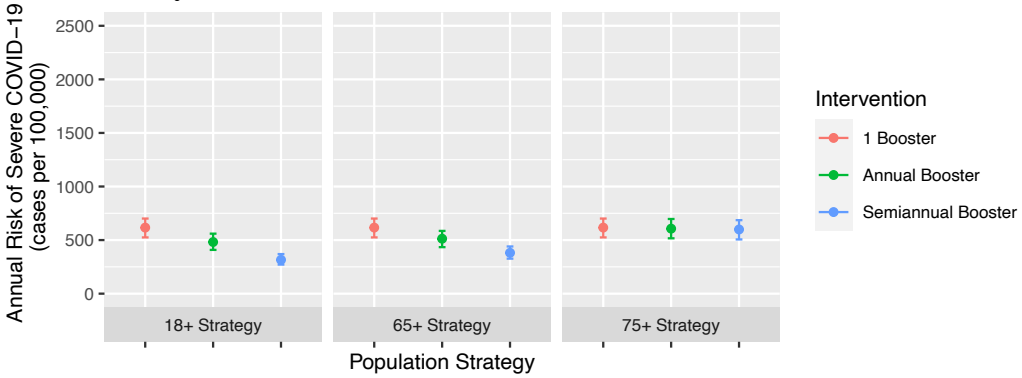
A. 18-49 years



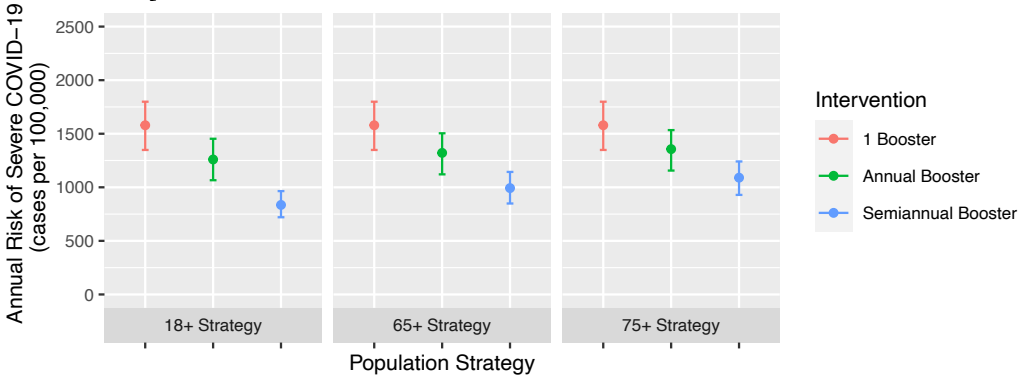
B. 50-64 years



C. 65-74 years



D. 75+ years



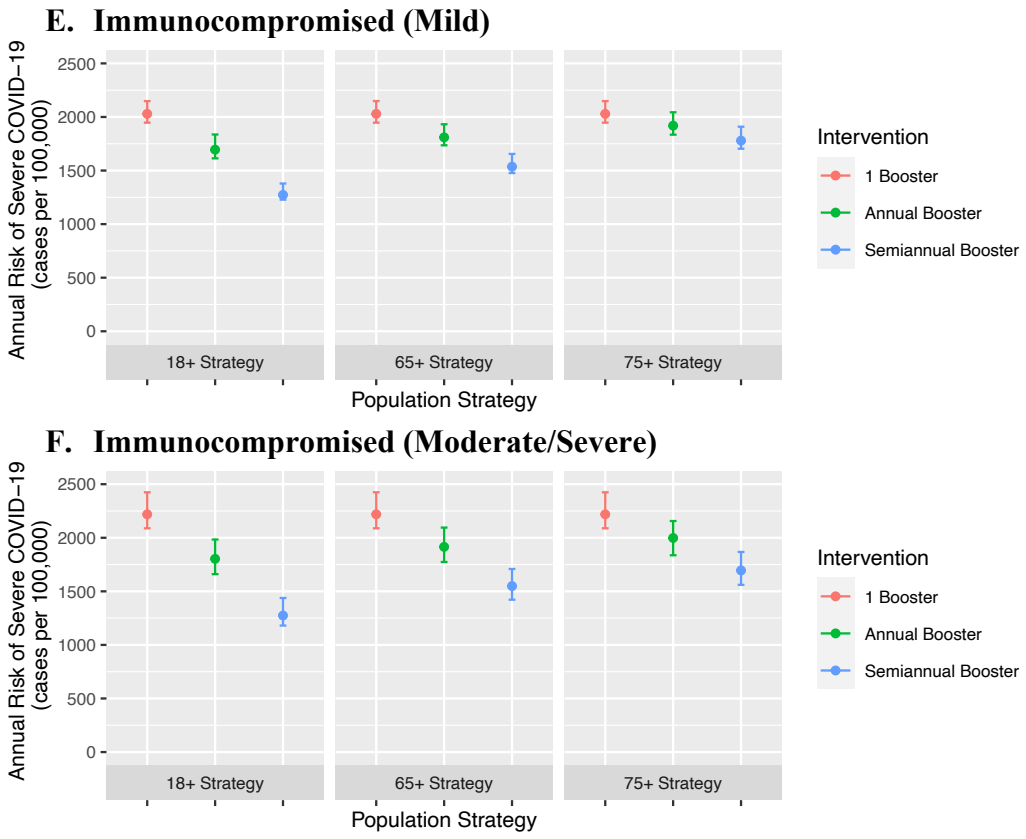


Figure S6: Scenario analysis using a dynamic transmission model under optimistic coverage assumptions to estimate the impact of indirect effects on COVID-19 booster vaccination strategies in four age groups and two immunocompromised groups. We used a dynamic transmission model to compare different frequencies of COVID-19 booster vaccine in the following groups: (A) 75+ years, moderate/severe immunocompromised group; (B) 65+ years and all immunocompromised groups; and (C) 18+ years in all groups. We assumed a background of one-time booster vaccination at the start of the simulation in adults (18+ years) with age-specific coverage based on optimistic uptake assumptions. We plotted absolute annual risk of severe COVID-19 over a two-year simulation in four age groups and two immunocompromised groups, to compare the indirect effects of booster vaccination on all risk groups. Table A7 reports the coverage estimates (optimistic vaccine uptake assumption).