

RSV Scenario Modeling Hub Report

26 February, 2024 Scenario Modeling Hub Team¹

Key Takeaways

Full scenario specifications can be found <u>here</u>.

In our first round of RSV projections, we generated mid-season hospitalization estimates for the 29-week period Nov 12, 2023 to June 1, 2024. We considered 4 intervention scenarios representing the impact of new interventions to mitigate the burden of RSV, along with a counterfactual "status quo" scenario where RSV control is the same as in past years. Intervention scenarios assumed optimistic and pessimistic levels of coverage and effectiveness of long-acting monoclonal antibodies (nirsevimab) in infants under 7 mo, combined with optimistic and pessimistic levels of coverage and effectiveness of vaccination in seniors 60+yrs. Scenario assumptions were indexed on past coverage of influenza vaccines by state and age group and efficacy estimates from randomized control trials for RSV interventions. Here we present ensemble projections based on contributions from 10 teams, using the trimmed linear opinion pool aggregation approach. All-age and age-specific estimates of RSV hospitalizations are provided nationally and for 12 states contributing to RSV-NET surveillance.

Our main findings include:

- RSV interventions, compared to a no-intervention scenario, would avert on average 11% (95% CI 6-16%) of RSV hospitalizations during the projection period based on our most optimistic assumptions (scenario A, optimistic intervention coverage and high effectiveness in both infants and seniors). This amounts to 15,500 average seasonal hospitalizations averted nationally (95%CI 9,300-21,600). These reductions would be 4% (95% CI 2-6%), or 6,200 (95% CI 3,600-8,900) average hospitalizations averted, with the most pessimistic assumptions (scenario D, pessimistic intervention coverage and moderate effectiveness in both infants and seniors).
- Intervention benefits are projected to be higher in the targeted age groups than overall. In the most optimistic scenario, an average of 21% (95% CI 16-24%) of RSV hospitalizations would be averted among seniors over 65 yrs and 15% (95% CI 4-24%) among infants under 1 yr. In this optimistic scenario, about 56% of total hospitalizations averted are projected to be in infants. These results correspond to 1.24 (95% CI 0.45-2.03) infant hospitalization averted per 100 doses of monoclonals delivered in 2023-24) and 0.04 (0.03-0.05) senior hospitalization averted per 100 vaccine doses.
- The peak and cumulative hospitalization burden of the 2023-24 RSV season is likely to remain lower than that of the last season which had seen a large and unusual post-COVID-19 rebound of RSV, especially in children. The projected peak in 2023-24 is somewhat higher than that of the last pre-pandemic season (2019-20). This is based on the 75% projection interval of all-age estimates.
- In our most optimistic scenario (scenario A, high intervention coverage and effectiveness in both infants and seniors), median weekly hospitalizations would peak at 11,200 (95% PI 4,400-25,900). In our most pessimistic scenario (scenario E, non-intervention counterfactual), weekly hospitalizations would peak at 12,100 (95% PI 5,900-28,700). Cumulative RSV hospitalizations for the period July 1, 2023-June 1, 2024 are projected to reach 168,000 (95,500-303,000) for the most optimistic scenario, and 183,000 (95%PI 106,000-315,000) for the counterfactual scenario.
- In all scenarios, ensemble projections suggest a prolonged period of RSV activity between November and March, with a peak most likely to occur in mid-December 2023. Based on the median of all contributing models and the ensemble, the national peak of RSV is projected to have passed at the time of writing of this report. There is heterogeneity in projected RSV timing between the 12 states considered in this analysis, with most likely peak dates ranging between Nov 15, 2023 (Georgia, Tennessee) and Jan 15, 2024 (Utah).
- The combined impact of RSV, influenza, and COVID-19 on hospitalizations is likely to remain below that of last season (2022-23). This result is based on the 75% projection interval combining prior projections generated by the scenario Modeling Hub for these 3 pathogens. We assume high immune escape for COVID-19 with moderate booster uptake in all age groups (https://covid19scenariomodelinghub.org/), dominance of the A/H1N1 influenza subtype with typical influenza vaccine coverage (https://fluscenariomodelinghub.org/), optimistic RSV interventions for seniors and infants

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(scenario A), and no interaction between respiratory viruses. COVID-19 is projected to remain the dominant pathogen contributing to respiratory hospitalizations throughout the season. Of note in 2022-23, there was concurrent activity of influenza, COVID-19, and RSV early in the season, resulting in a particularly high total hospitalization burden. Activity of these pathogens is projected to be more asynchronous this year.

There is variability between states in the projected timing and intensity of RSV activity this season. This variability is
due in part to geographic differences in the seasonality of RSV, the impact of COVID-19 NPIs since 2020, and potential
differences in testing and transmission intensities.

A few caveats are worth noting:

- There are differences in the post-pandemic rebound of RSV across age groups, which are not fully understood nor accounted for by all models. In particular, projections tend to underestimate disease burden in seniors. These differences could be in part due to different strengths of NPIs between young children and adults during the COVID19 period (including masking propensities), along with age-specific changes in RSV reporting.
- Based on recent data on RSV intervention uptake in the US, our optimistic scenario A seems most closely aligned with reality, though data on infant monoclonal uptake are incomplete at this time.
- This is the first round of RSV projections, and there is limited availability of calibration data or past RSV modeling experience. This is the first time that the RSV-NET hospitalization dataset has been used for long-term projections. RSV-NET covers a fraction of 12 states (9% of the US population overall) and the amount of retrospective data is limited. Further, few auxiliary datasets are available for RSV calibration, particularly regarding infections.
- Most models assume that RSV interventions will not reduce infection or transmission, so that indirect benefits are close to zero in ensemble estimates. Further, based on our optimistic scenario assumptions, the maximum reductions that would be expected from RSV interventions this season would be 21% for infants and 25% for seniors, in the hypothetical situation where intervention coverage had reached saturation before the start of the RSV season. Our ensemble projections based on the dynamics of RSV epidemics and a realistic roll-out of interventions suggest somewhat lower benefits (15 and 21% in infants and seniors, respectively), likely due to a small amount of interventions delivered too late with respect to the timing of the RSV season.
- Testing practices continue to evolve in the wake of the COVID19 pandemic, including increased use of multi-pathogen testing in clinical settings, which may affect reported hospitalizations in the RSV-NET system. This in turn will affect comparison with our projections and with prior year hospitalization data.
- We have presented the trimmed LOP as our default for ensembling, but results for the untrimmed LOP are shown on the website.

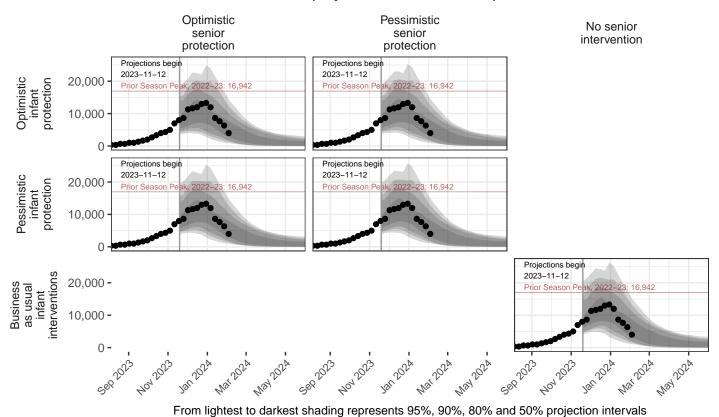
Round 1 - 2023-2024 Scenario Specifications

RSV Round 1 considered 4 intervention scenarios representing the impact of new interventions to mitigate the burden of RSV, plus 1 counterfactual "status quo" scenario with RSV control the same as in past years (assuming new vaccines and monoclonal antibodies were not available in 2023-24). Intervention scenarios assumed (1) optimistic and pessimistic coverage and effectiveness of long-acting monoclonal antibodies (nirsevimab) in infants under 7 months, and (2) optimistic and pessimistic coverage and effectiveness of vaccination in seniors 60+ years. Scenario assumptions are indexed on past coverage of influenza vaccines by state and age group and efficacy estimates from randomized control trials for RSV interventions.

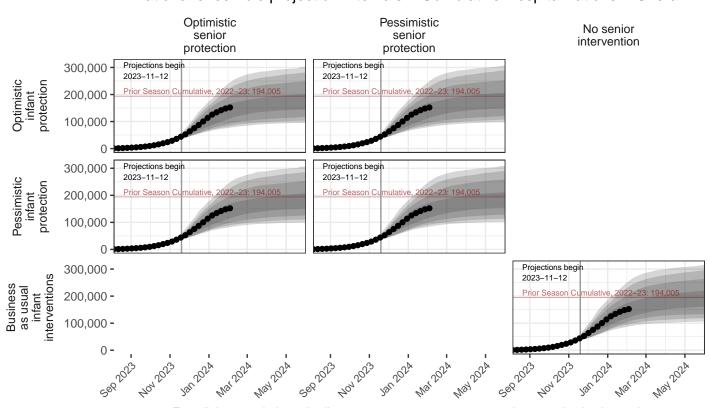
	Optimistic senior protection Vaccine is administered from Sep-June to seniors 60+ yrs - coverage saturates at 40% of the 2021-22 state- and age-specific flu vaccine coverage - VE against hospitalization is 90%	Pessimistic senior protection Vaccine is administered from Sep-June to seniors 60+ yrs - coverage saturates at 20% of the 2021-22 state-and age-specific flu vaccine coverage - VE against hospitalization is 70%	No senior intervention
Optimistic infant protection Long-acting monoclonals target infants < 6 months during RSV season (Oct-Mar) - coverage saturates at 60% of the 2021-22 state- and age-specific flu vaccine coverage - VE against hospitalization is 80%	Scenario A	Scenario B	
Pessimistic infant protection Long-acting monoclonals target infants < 6 months during RSV season (Oct-Mar) -coverage saturates at 20% of the 2021-22 state- and age-specific flu vaccine coverage - VE against hospitalization is 60%	Scenario C	Scenario D	
No infant intervention beyond what was used in prior years (limited supply of palivizumab, targeting ~2% of birth cohort at high risk)			Scenario E (counterfactual)

Full scenario specifications can be found $\underline{\text{here}}$.

National ensemble projection intervals – Hospitalizations – Overall



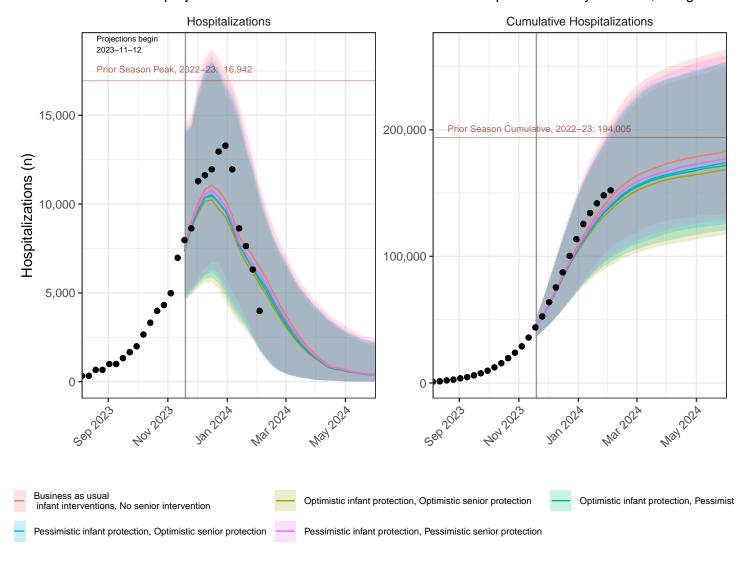
National ensemble projection intervals - Cumulative Hospitalizations - Overall



Scenario Comparison

The scenario projections were overall very similar between scenarios, with increased peak and cumulative size as scenarios became more pessimistic. The national projections also follow the empirical hospitalizations well for both incident and cumulative projections, demonstrating robustness and good calibration of the overall ensemble. Horizontal lines are given for prior peak incident and cumulative hospitalizations from the 2022-23 season, taken from RSV-NET (which is used as a proxy for hospitalizations).

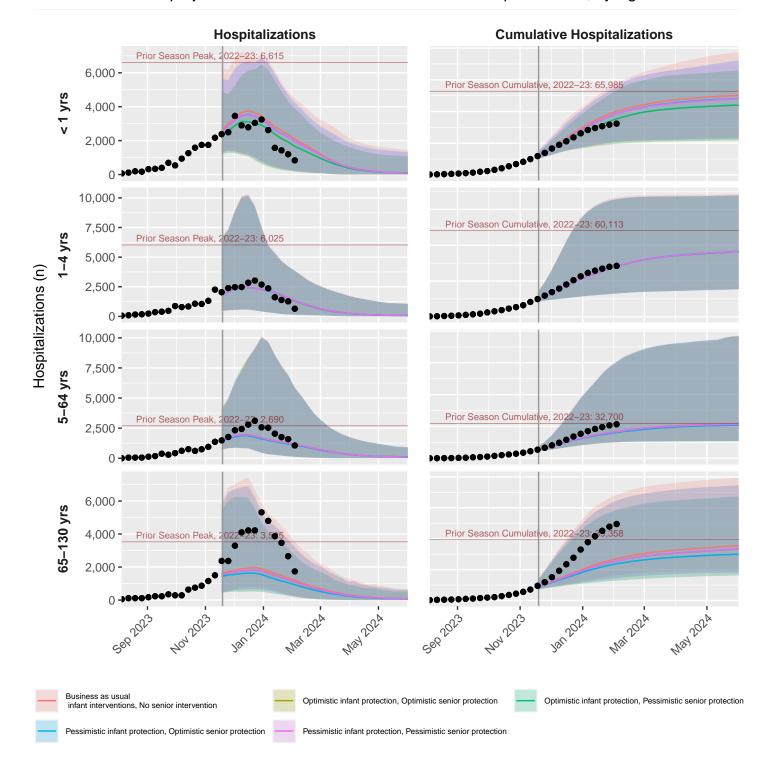
Ensemble projections for national incident and cumulative hospitalizations by scenario, all ages.



Comparisons by Age

The scenario projections by age group were also very similar between scenarios nationally, with increased peak and cumulative size as scenarios became more pessimistic. The national projections also follow the empirical age-specific hospitalizations well for the younger age groups, however, there is significant under-projection of hospitalizations in the 65-130 year age group, though the 95% projection intervals of the cumulative do contain the empirical data. This age group also substantially exceeded both peak and cumulative hospitalizations from the 2022-23 season, which was considered substantially larger; this may indicate a change in testing or reporting among this age group, and not a difference in infection or disease. Horizontal lines are given for prior peak incident and cumulative hospitalizations from the 2022-23 season, taken from RSV-NET (which is used as a proxy for hospitalizations). Lines represent the median ensemble projections, and shaded regions represent the 95% prediction intervals.

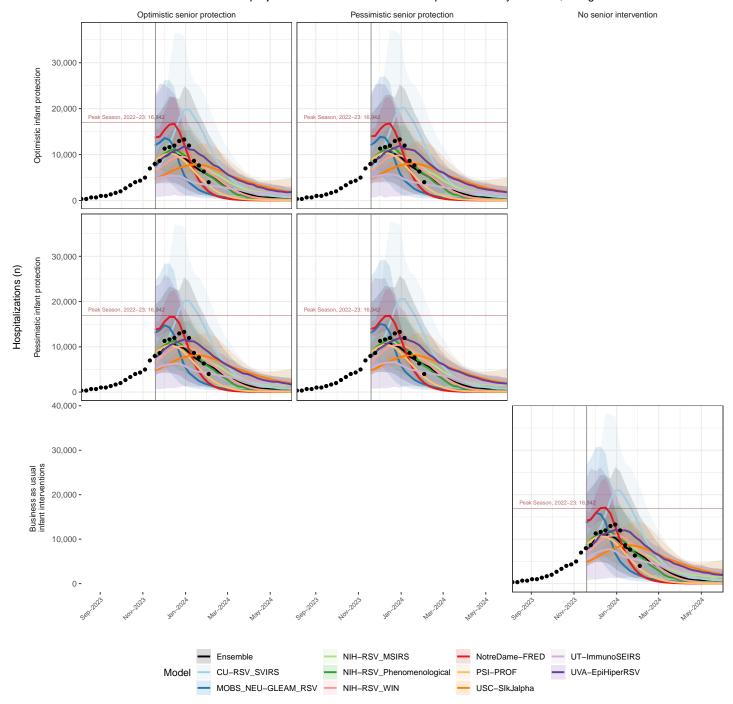
National ensemble projections of incident and cumulative RSV hospitalizations, by Age



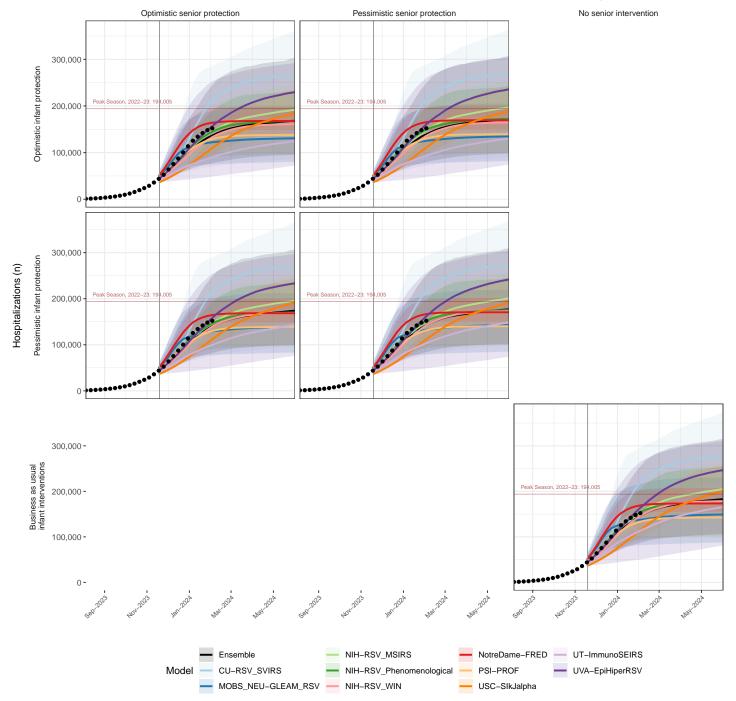
National individual model projections

 $Individual\ model\ projections\ and\ ensemble\ by\ scenario\ for\ national\ hospitalizations,\ deaths\ and\ cumulative\ hospitalizations.$

Ensemble projections for national incident hospitalizations by scenario, all ages.

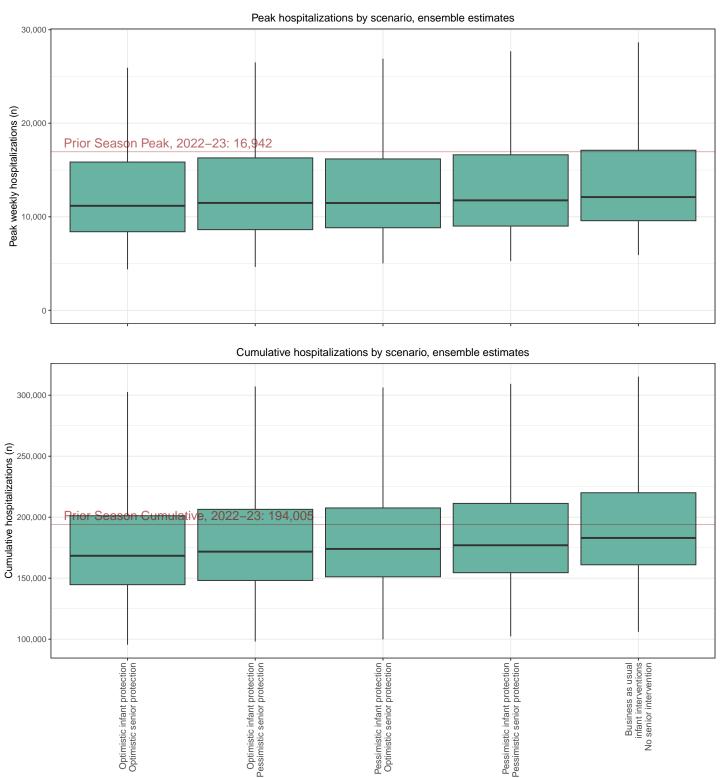


Ensemble projections for national cumulative hospitalizations by scenario, all ages.



Peak and Cumulative Hospitalizations

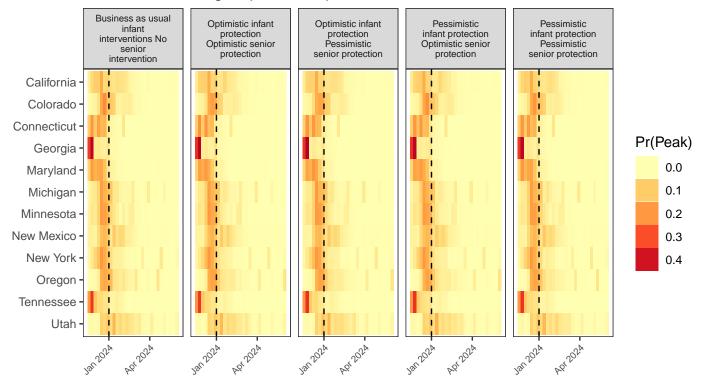
Scenario variation in national peak size and cumulative hospitalization burden



Peak hospitalization timing

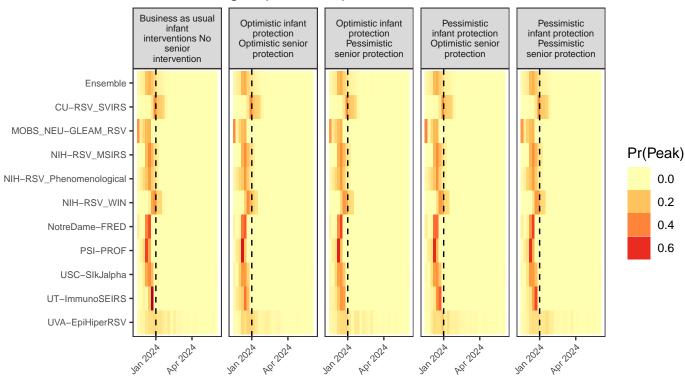
State variability in peak hospitalization timing. Ensemble projections of state-level timing of peak hospitalization incidence.

Timing of peak hospitalization across states



Model variability in national peak hospitalization timing. Individual model probabilities for national timing of peak hospitalizations.

Timing of peak hospitalization across models

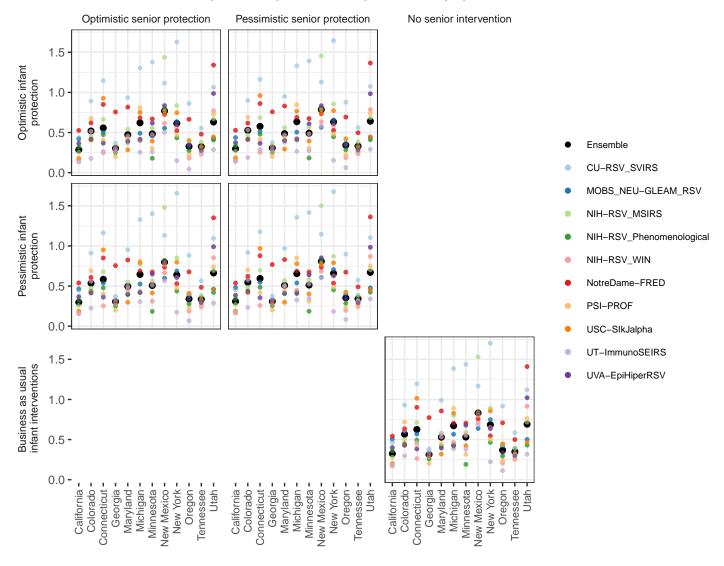


Peak hospitalization size

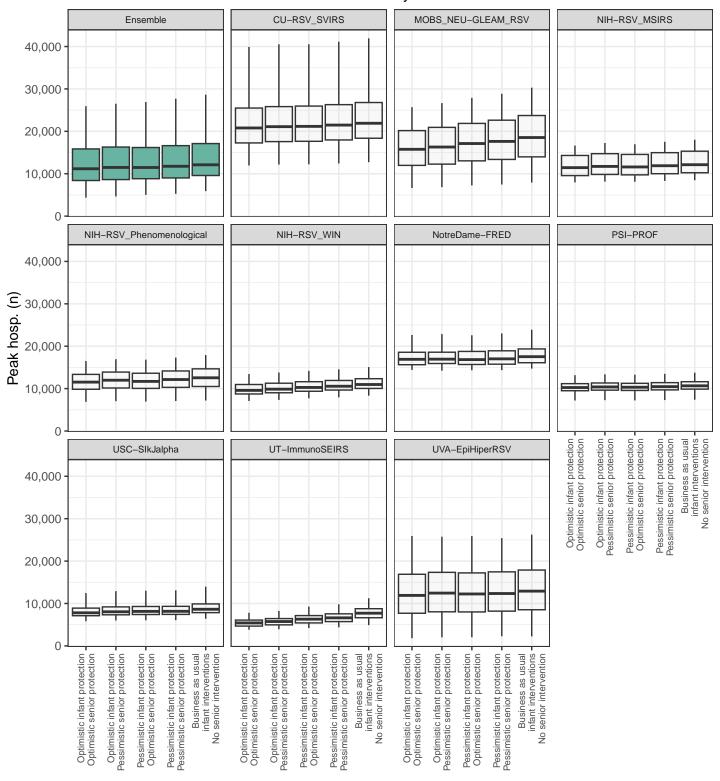
Variability in peak hospitalization incidence, by state and model.

Individual model and ensemble projections for state-level weekly peak hospitalization incidence per 10,000 population.

State variation in peak hospitalizations per 10,000 population



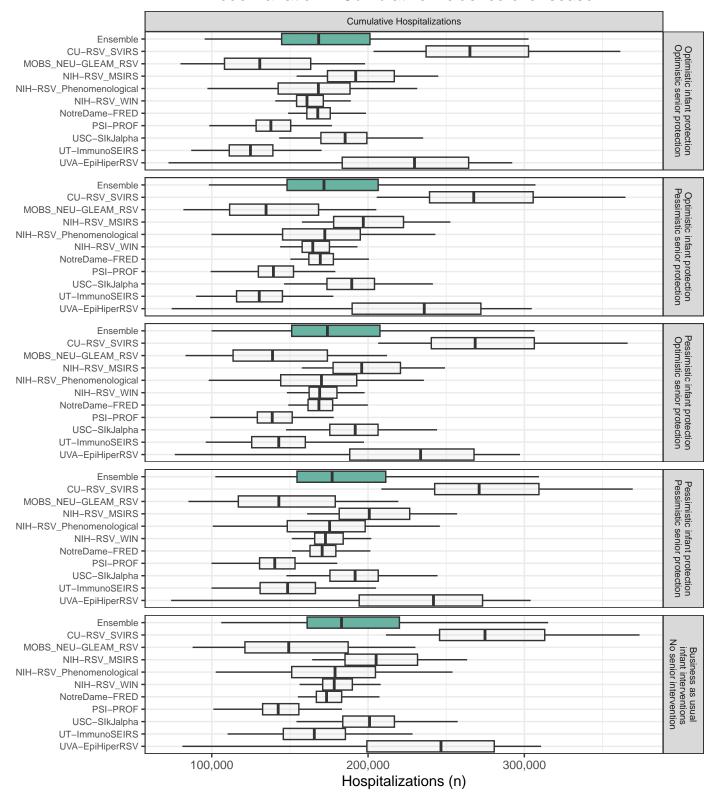
Peak size by model



Cumulative Hospitalizations

Cumulative incidence over season by model

Model variation - Cumulative incidence over season



Risk Maps, Peak and Cumulative Hospitalization Rates

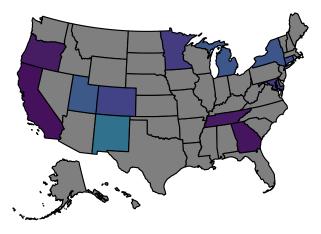
Peak Hospitalizations per 10,000 population

Cumulative Hospitalizations per 10,000 population

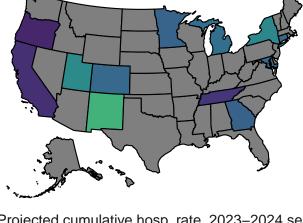
Projected cumulative hosp. rate, 2023–2024 seas

Optimistic infant protection, Optimistic senior protection

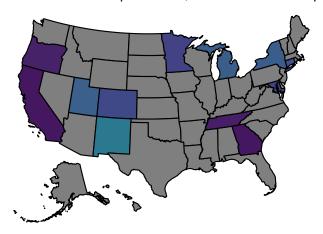
Projected peak size for 2023–2024 season, Optimistic infant protection, Optimistic senior protection



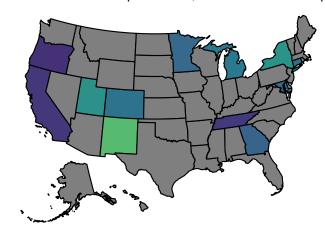
Projected peak size for 2023–2024 season, Pessimistic infant protection, Pessimistic senior pi



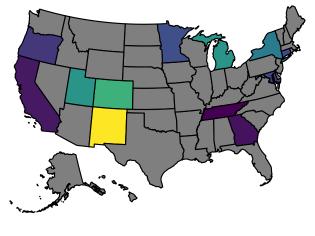
Projected cumulative hosp. rate, 2023–2024 seas Pessimistic infant protection, Pessimistic senior pr



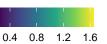
Reported peak size, 2022–2023 season

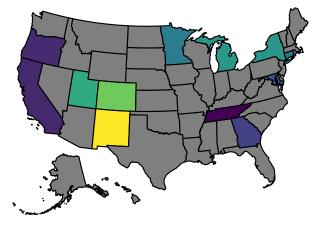


Reported cumulative hosp. rate, 2022–2023 seas

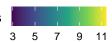


Peak incident hosps per 10,000 pop





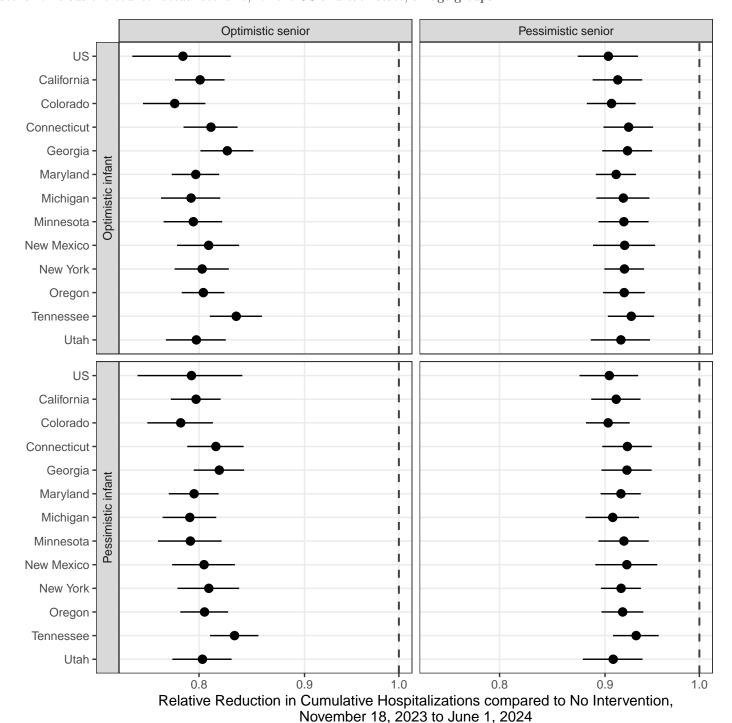
Cumulative hosps per 10,000 pop



Meta-Analysis of Scenario Comparative Impacts - National

Relative Reduction in Hospitalization compared to No Intervention (the Counterfactual)

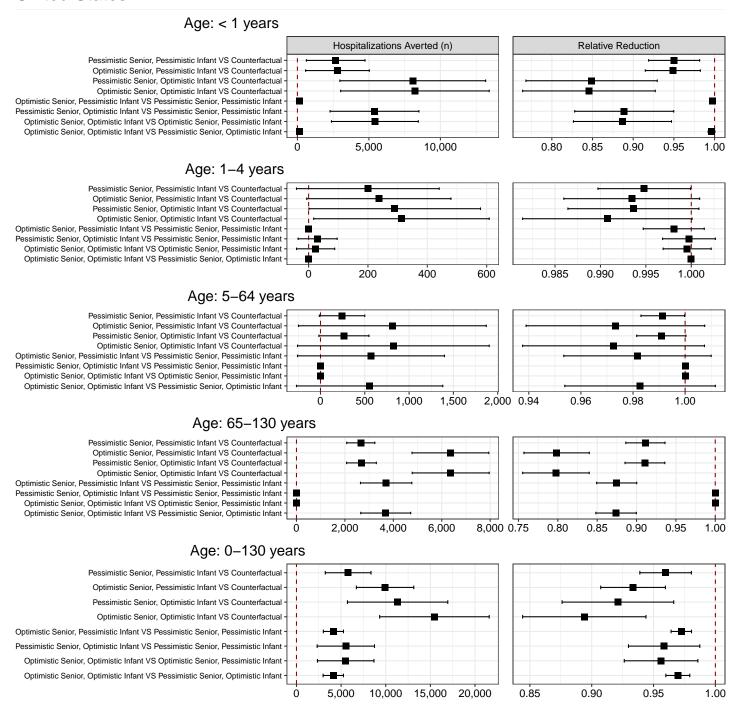
Estimates of relative hospitalizations averted contrasting cumulative projections at the end of the season for each vaccine scenario versus the counterfactual scenario, for the US and each state, all age groups.



National Impact of RSV Immunization Scenarios, by Age

Estimates of cumulative hospitalizations averted and relative reduction in hospitalization for November 18, 2023 to June 1, 2024 comparing scenarios, for the US, by age group.

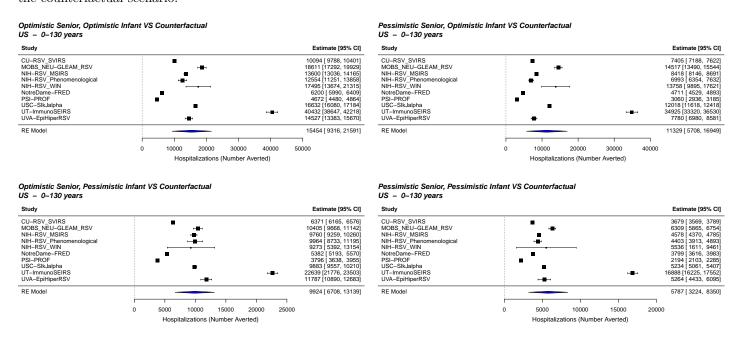
United States



National Estimates of Hospitalizations averted by Infant and Senior Immunization as compared to the Counterfactual

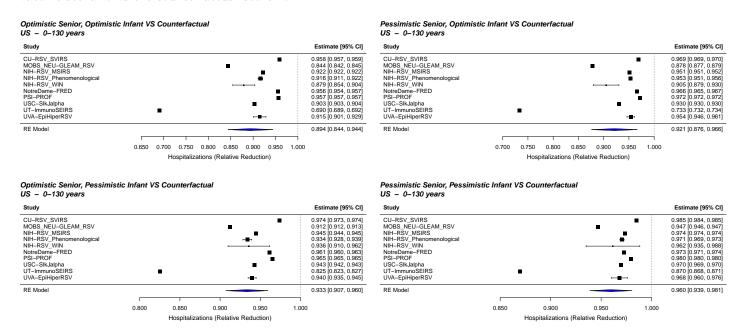
Number of Hospitalizations Averted

Estimates of hospitalizations averted contrasting cumulative projections at the end of the season for each vaccine scenario vs the counterfactual scenario.



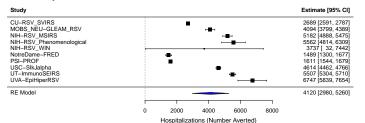
Relative Reduction in Hospitalizations

Estimates of the relative reduction in hospitalization contrasting cumulative projections at the end of the season for each vaccine scenario vs the counterfactual scenario.

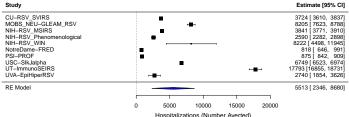


National Estimates of Hospitalizations averted by Optimistic vs Pessimistic Immunization Number of Hospitalizations Averted

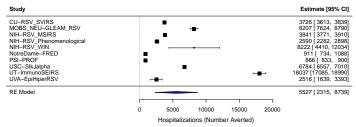
Optimistic Senior, Optimistic Infant VS Pessimistic Senior, Optimistic Infant US - 0-130 years



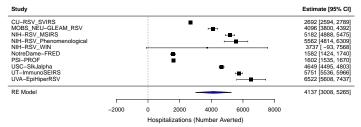
Optimistic Senior, Optimistic Infant VS Optimistic Senior, Pessimistic Infant US - 0-130 years



Pessimistic Senior, Optimistic Infant VS Pessimistic Senior, Pessimistic Infant US - 0-130 years

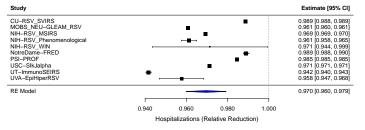


Optimistic Senior, Pessimistic Infant VS Pessimistic Senior, Pessimistic Infant US - 0-130 years

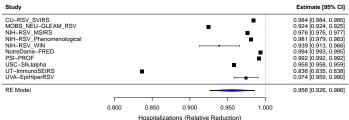


Relative Reduction in Hospitalizations

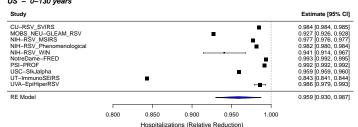
Optimistic Senior, Optimistic Infant VS Pessimistic Senior, Optimistic Infant US - 0-130 years



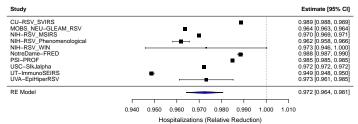
Optimistic Senior, Optimistic Infant VS Optimistic Senior, Pessimistic Infant US = 0–130 years



Pessimistic Senior, Optimistic Infant VS Pessimistic Senior, Pessimistic Infant US - 0-130 years



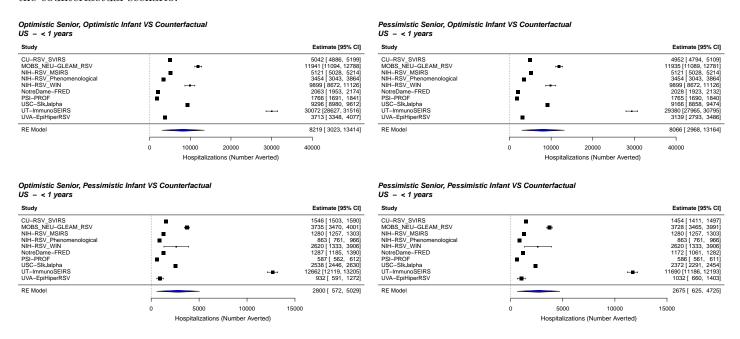
Optimistic Senior, Pessimistic Infant VS Pessimistic Senior, Pessimistic Infant US - 0-130 years



Infants: National Estimates of Hospitalizations averted by Infant and Senior Immunization as compared to the Counterfactual

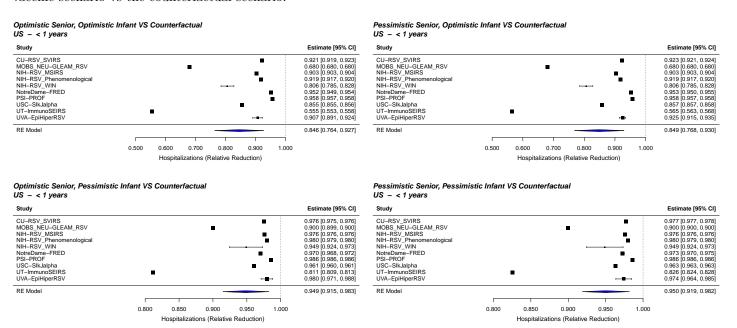
Number of Hospitalizations Averted Among Infants (0 - 0.99 yrs)

Estimates of hospitalizations averted contrasting cumulative projections at the end of the season for each vaccine scenario vs the counterfactual scenario.



Relative Reduction in Hospitalizations Among Infants (0 - 0.99 yrs)

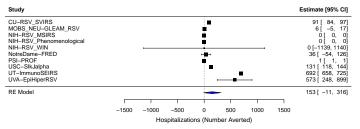
Estimates of the relative reduction in hospitalization contrasting cumulative projections at the end of the season for each vaccine scenario vs the counterfactual scenario.



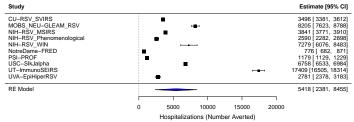
Infants: National Estimates of Hospitalizations averted by Optimistic vs Pessimistic Immunization

Number of Hospitalizations Averted Among Infants (0 - 0.99 yrs)

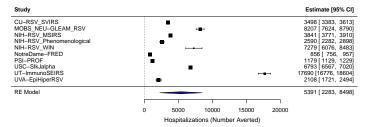
Optimistic Senior, Optimistic Infant VS Pessimistic Senior, Optimistic Infant US - < 1 years



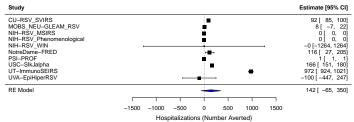
Optimistic Senior, Optimistic Infant VS Optimistic Senior, Pessimistic Infant US - < 1 years



Pessimistic Senior, Optimistic Infant VS Pessimistic Senior, Pessimistic Infant

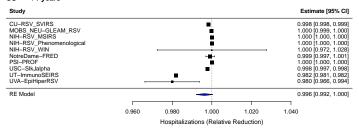


Optimistic Senior, Pessimistic Infant VS Pessimistic Senior, Pessimistic Infant US - < 1 years

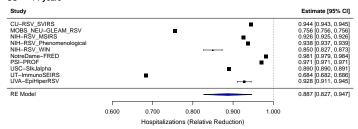


Relative Reduction in Hospitalizations Among Infants (0 - 0.99 yrs)

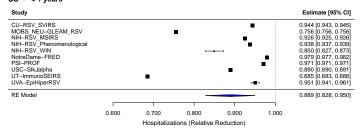
Optimistic Senior, Optimistic Infant VS Pessimistic Senior, Optimistic Infant US - < 1 years



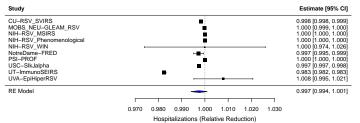
Optimistic Senior, Optimistic Infant VS Optimistic Senior, Pessimistic Infant US - < 1 years



Pessimistic Senior, Optimistic Infant VS Pessimistic Senior, Pessimistic Infant



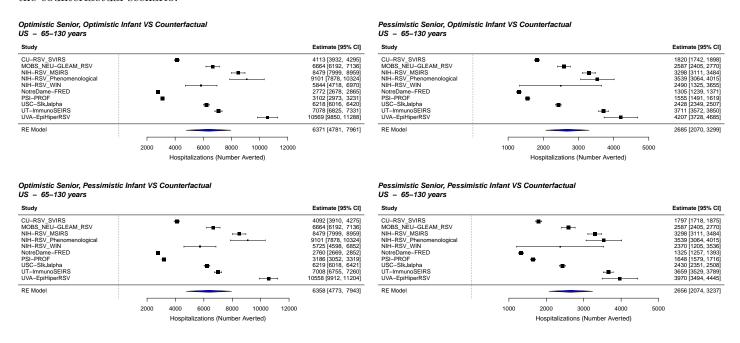
Optimistic Senior, Pessimistic Infant VS Pessimistic Senior, Pessimistic Infant US $\,-$ < 1 years



Seniors: National Estimates of Hospitalizations averted by Infant and Senior Immunization as compared to the Counterfactual

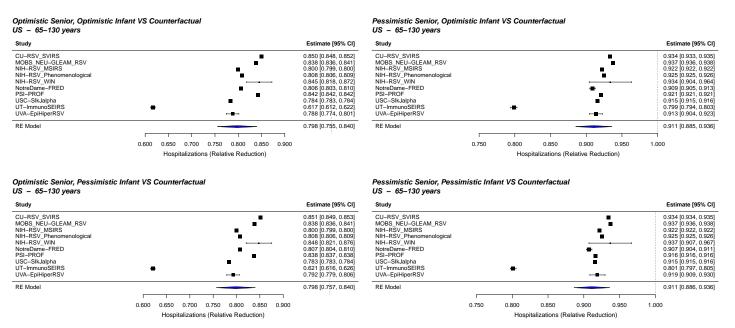
Number of Hospitalizations Averted Among Seniors (65 - 130 yrs)

Estimates of hospitalizations averted contrasting cumulative projections at the end of the season for each vaccine scenario vs the counterfactual scenario.



Relative Reduction in Hospitalizations Among Seniors (65 - 130 yrs)

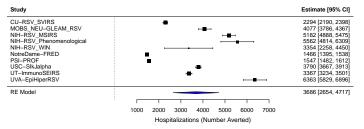
Estimates of the relative reduction in hospitalization contrasting cumulative projections at the end of the season for each vaccine scenario vs the counterfactual scenario.



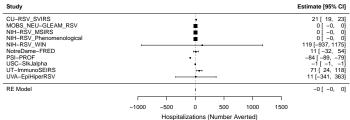
Seniors: National Estimates of Hospitalizations averted by Optimistic vs Pessimistic Immunization

Number of Hospitalizations Averted Among Seniors (65 - 130 yrs)

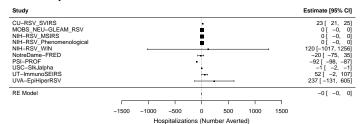
Optimistic Senior, Optimistic Infant VS Pessimistic Senior, Optimistic Infant US - 65–130 years



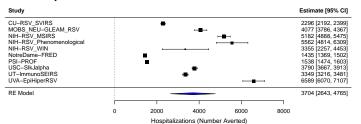
Optimistic Senior, Optimistic Infant VS Optimistic Senior, Pessimistic Infant US - 65-130 years



Pessimistic Senior, Optimistic Infant VS Pessimistic Senior, Pessimistic Infant US – 65–130 years

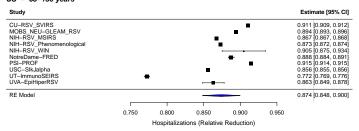


Optimistic Senior, Pessimistic Infant VS Pessimistic Senior, Pessimistic Infant US – 65–130 years

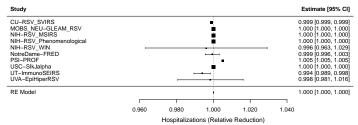


Relative Reduction in Hospitalizations Among Seniors (65 - 130 yrs)

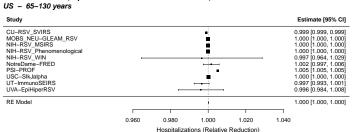
Optimistic Senior, Optimistic Infant VS Pessimistic Senior, Optimistic Infant US - 65-130 years



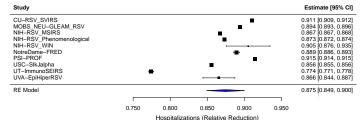
Optimistic Senior, Optimistic Infant VS Optimistic Senior, Pessimistic Infant US - 65-130 years



Pessimistic Senior, Optimistic Infant VS Pessimistic Senior, Pessimistic Infant



Optimistic Senior, Pessimistic Infant VS Pessimistic Senior, Pessimistic Infant US - 65-130 years



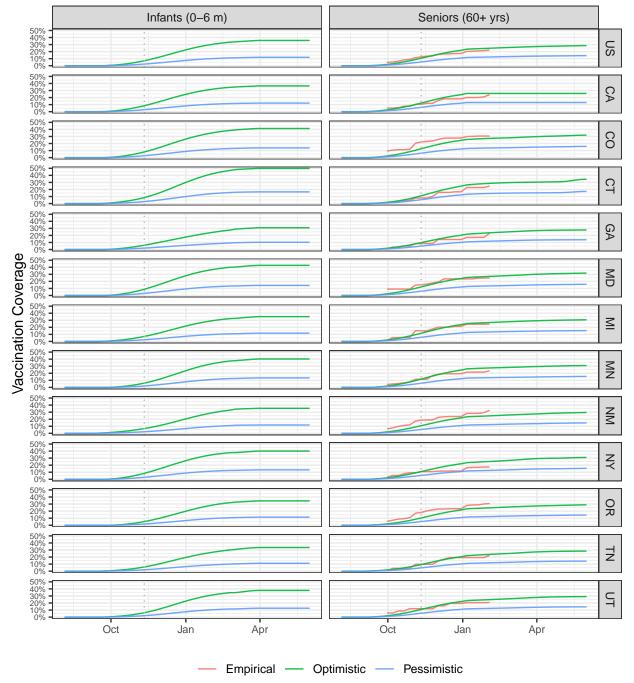
Scenarios VS Reality

How well do our scenarios match up with reality?

Answer: It Depends on the state and age group, but generally reality appears to match with Scenario A overall.

Senior vaccination coverage appears to be similar to the "optimistic" scenario, and always higher than pessimistic. However, data on the empirical infant vaccination coverage currently remain uncertain, and thus we have excluded them from the figure below. The CDC provides two sources of data for infant Nirsevimab coverage which contradict each other sharply. Current estimates from the National Immunization Survey (NIS) put national coverage at around 40% among infants <8 months (Jan 2024). However, these survey estimates have notable caveats and potential biases. In contrast, estimates from the Immunization Immunization System (ISS) are much more pessimistic, falling in line with or below the "pessimistic" scenario (\sim 10% coverage). These data also have substantial problematic caveats, specifically that they do not include infants born on or after October 1, 2023. See data and details on CDC's RSV Vax View. Based on these caveats, we believe the NIS coverage at \sim 40% in January 2024 may be more accurate, which puts reality close to the "optimistic" infant scenario.

Empirical vs Scenario Vaccination Coverages



Teams and models

- Columbia University RSV SVIRS
- Teresa Yamana, Sen Pei
- Fogarty International Center, National Institutes of Health (NIH) RSV_MSIRS
- Kaiyuan Sun, Cécile Viboud
- Fogarty International Center, National Institutes of Health (NIH) RSV_Phenomenological
- Kaiyuan Sun, Cécile Viboud
- Fogarty International Center, National Institutes of Health (NIH) RSV_WIN
- Samantha Bents, Chelsea Hansen, Cécile Viboud
- Northeastern University MOBS Lab GLEAM RSV
- Alessandro Vespignani, Matteo Chinazzi, Jessica T. Davis, Clara Bay, Guillaume St-Onge
- \bullet Predictive Science M2
- James Turtle, Michal Ben-Nun, Pete Riley
- University of Notre Dame FRED
- Sean Moore, Alex Perkins, Guido Espana
- University of Southern California SIkJalpha
- Ajitesh Srivastava, Majd Al Aawar
- University of Texas at Austin UT-ImmunoSEIRS
- Kaiming Bi (UT-Austin), Spencer J. Fox (University of Georgia), Shraddha R Bandekar (UT-Austin), Anass Bouchnita (UT-El Paso), Lauren Ancel Meyers (UT-Austin)
- University of Virginia Biocomplexity Institute FluXSim
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The RSV Scenario Modeling Hub Coordination Team

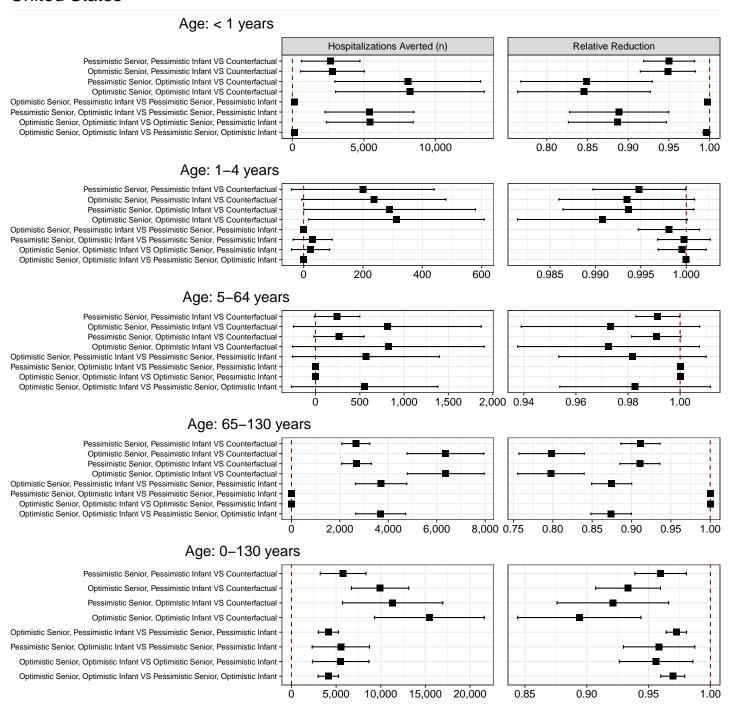
- Shaun Truelove, Johns Hopkins University
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- Sara Loo, Johns Hopkins University
- Lucie Contamin, University of Pittsburgh
- Emily Howerton, Penn State University
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- Harry Hochheiser, University of Pittsburgh
- Katriona Shea, Penn State University
- Michael Runge, USGS
- Erica Carcelen, Johns Hopkins University
- Sung-mok Jung, University of North Carolina
- J Espino, University of Pittsburgh
- John Levander, University of Pittsburgh

Supplementary Information

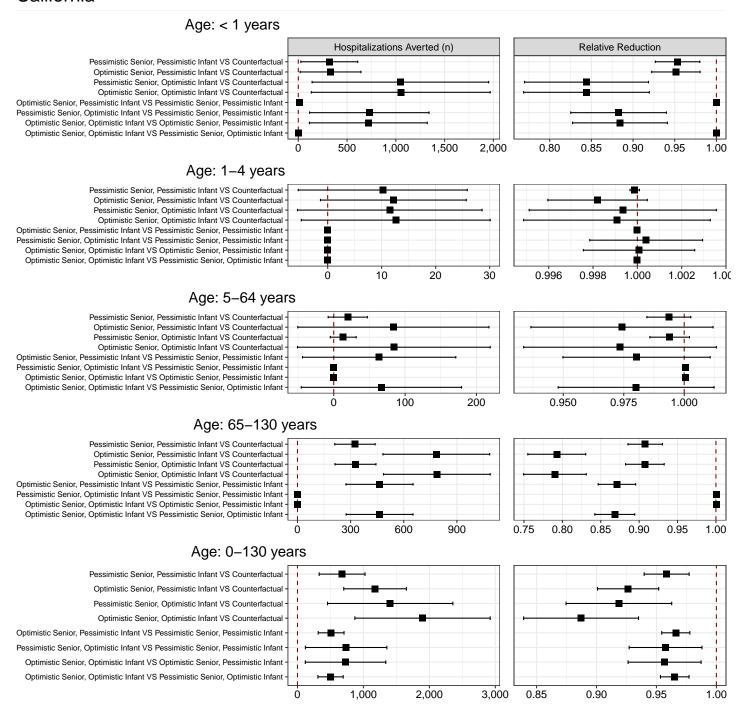
State Impact of RSV Immunization Scenarios, by Age

Estimates of cumulative hospitalizations averted and relative reduction in hospitalization for November 18, 2023 to June 1, 2024 comparing scenarios, for the each state, by age group.

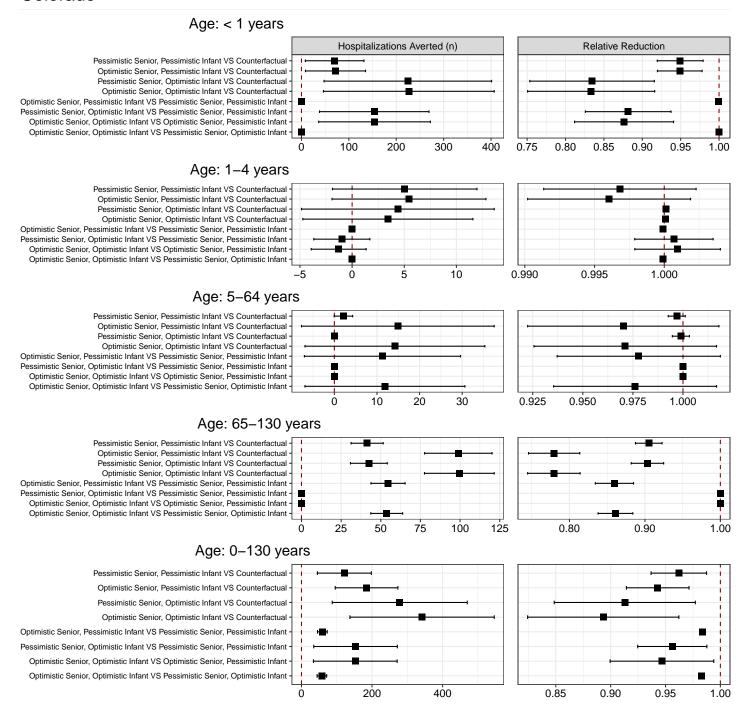
United States



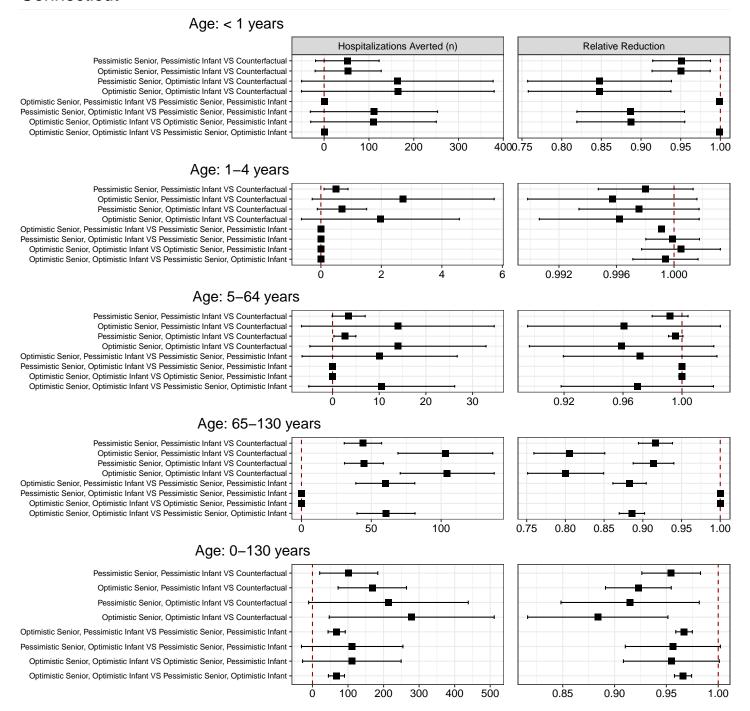
California



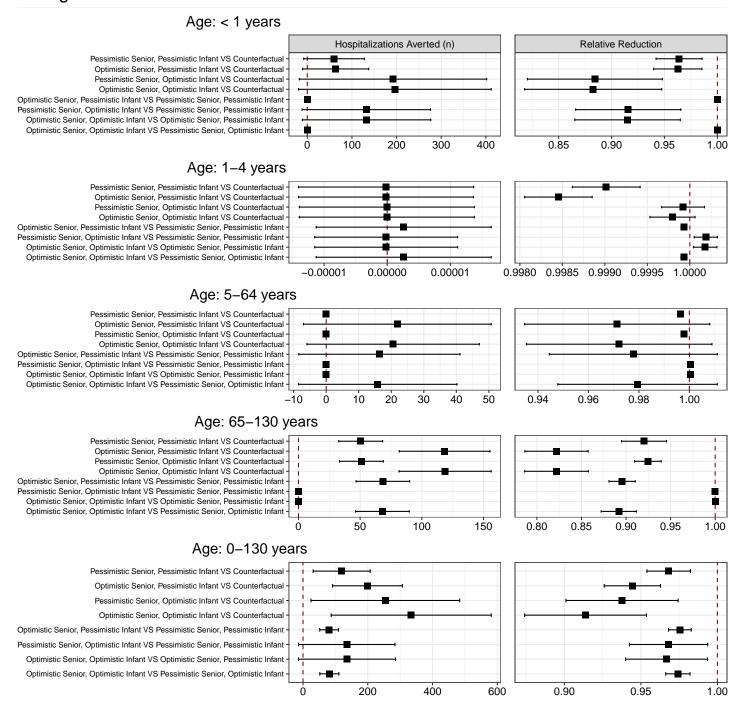
Colorado



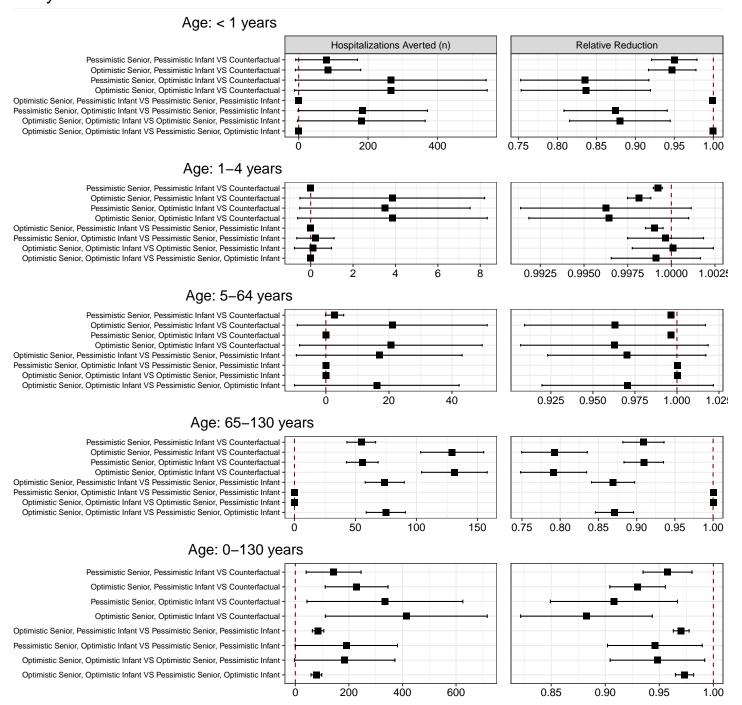
Connecticut



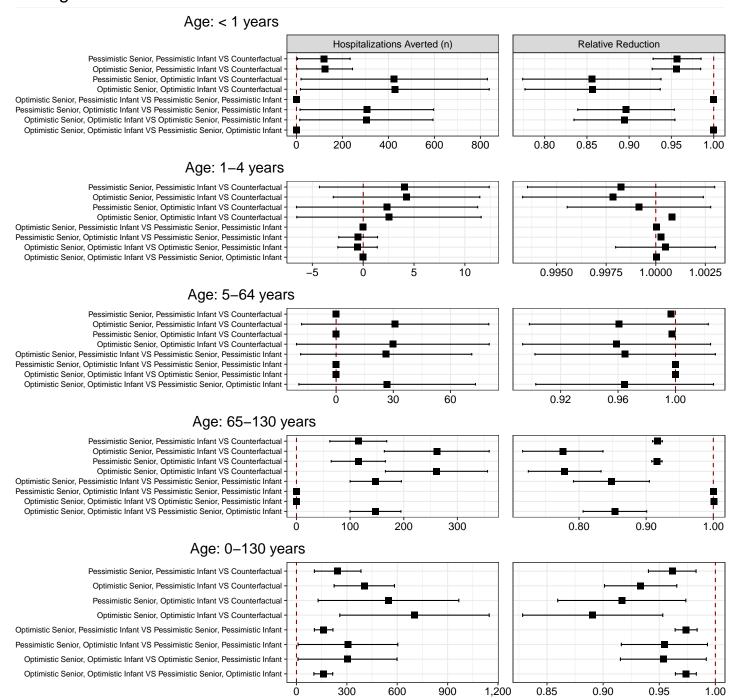
Georgia



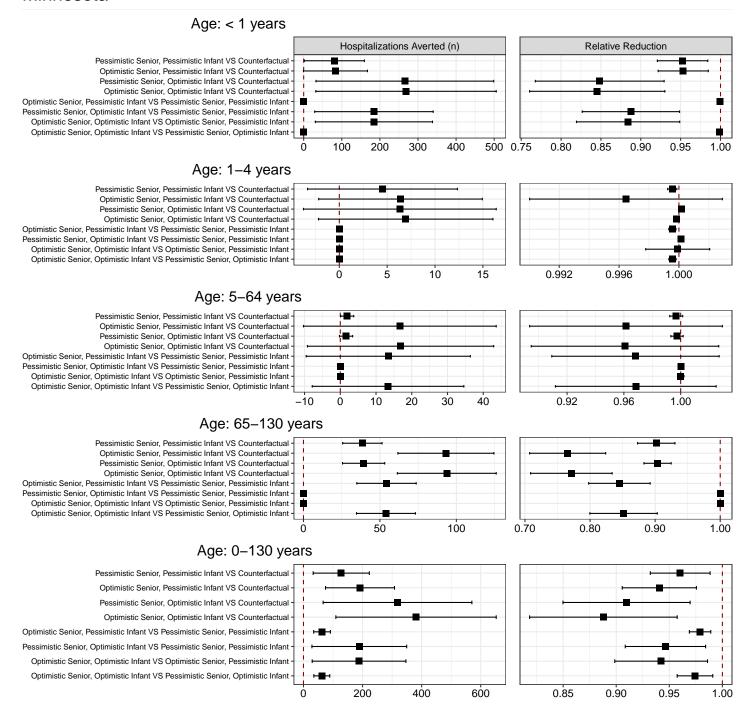
Maryland



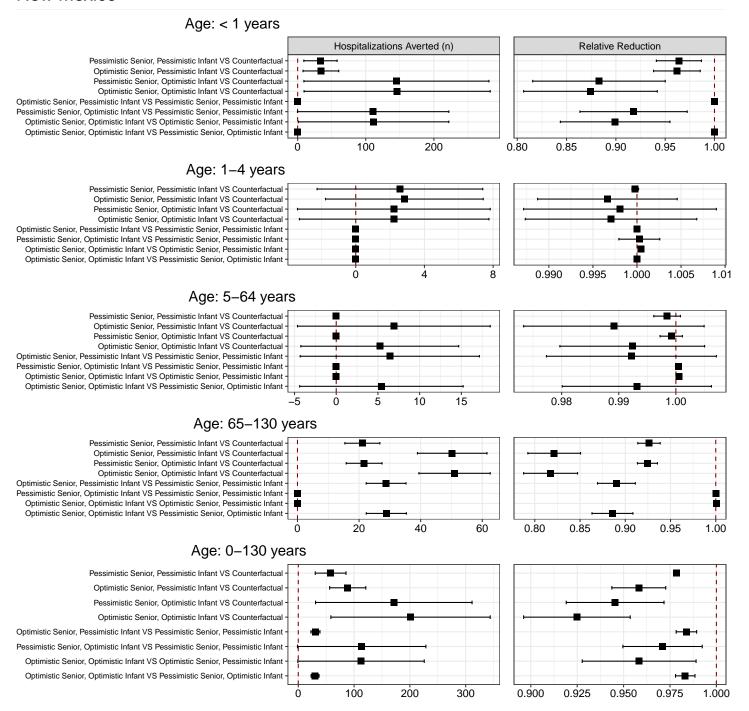
Michigan

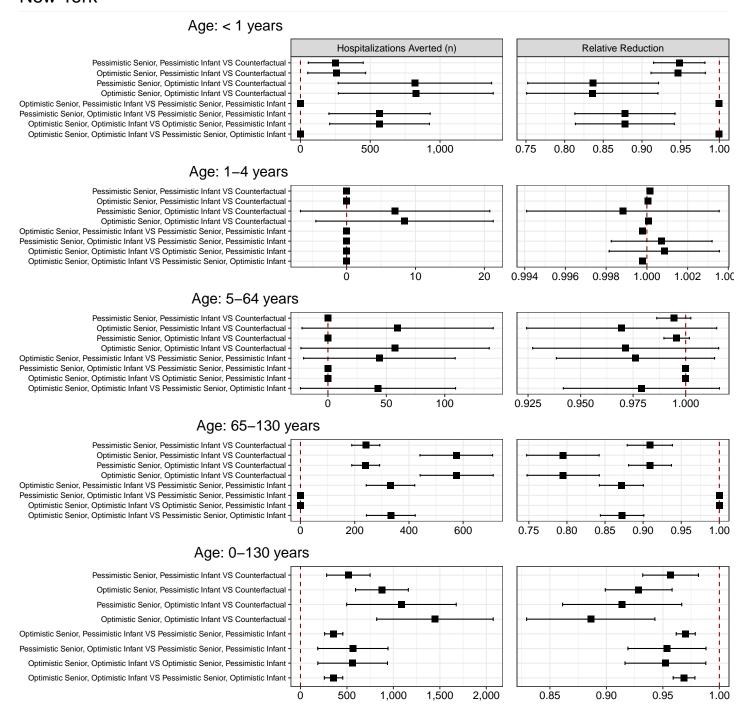


Minnesota

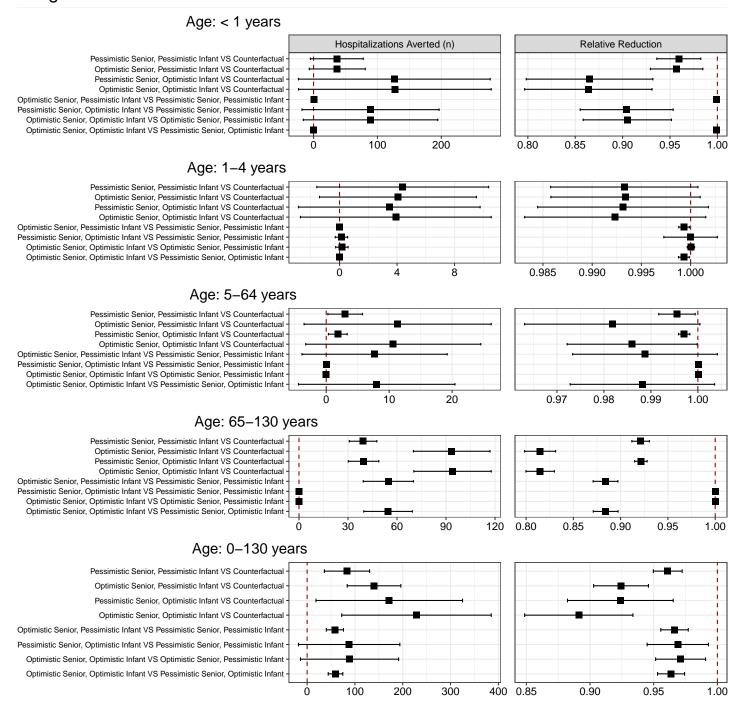


New Mexico

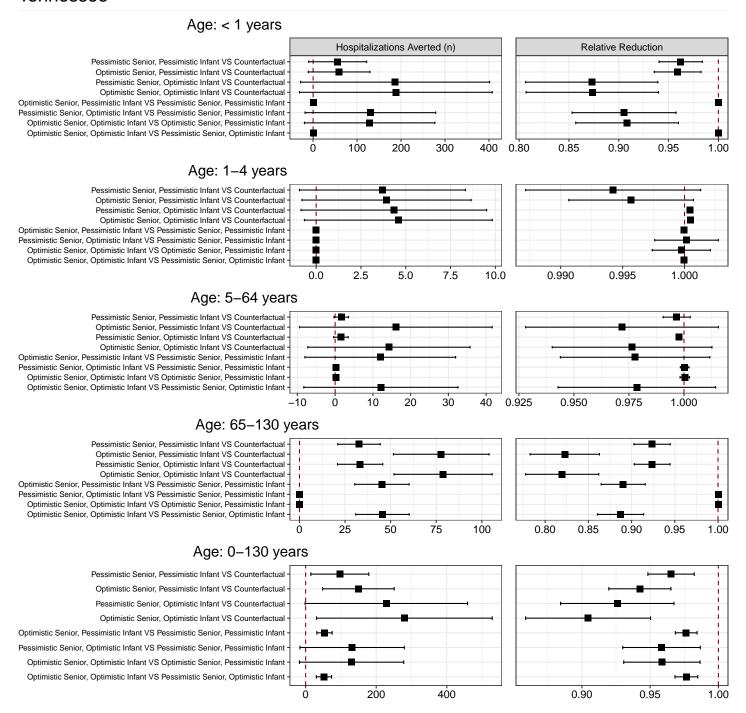




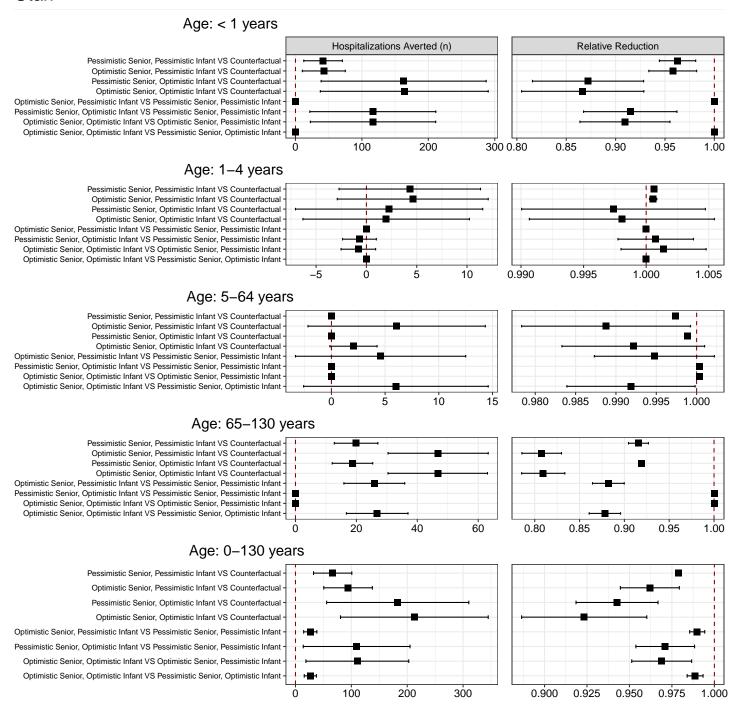
Oregon



Tennessee

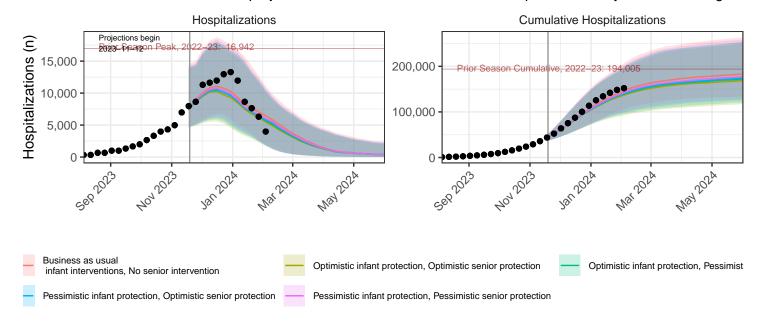


Utah

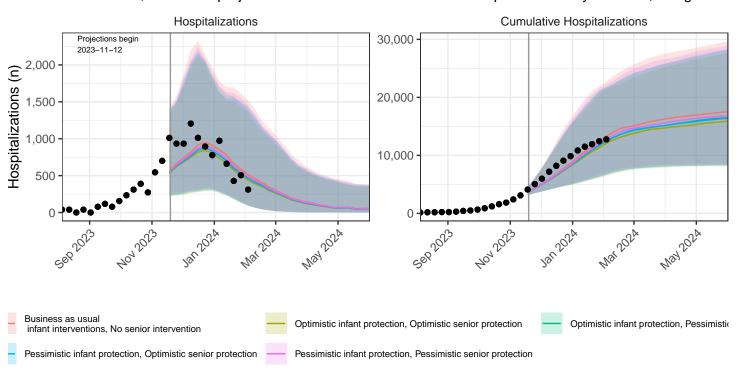


State Scenario Comparison

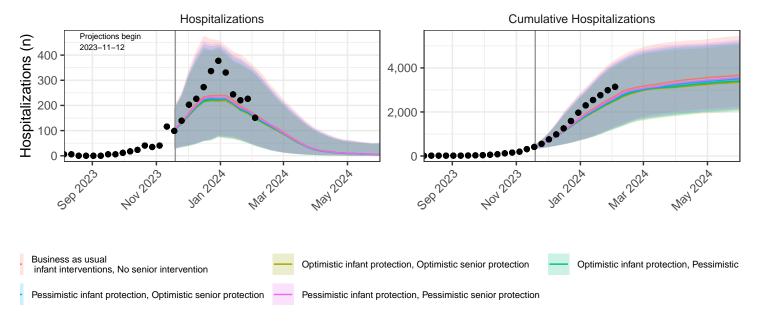
United States, Ensemble projections for incident and cumulative hospitalizations by scenario, all ages.



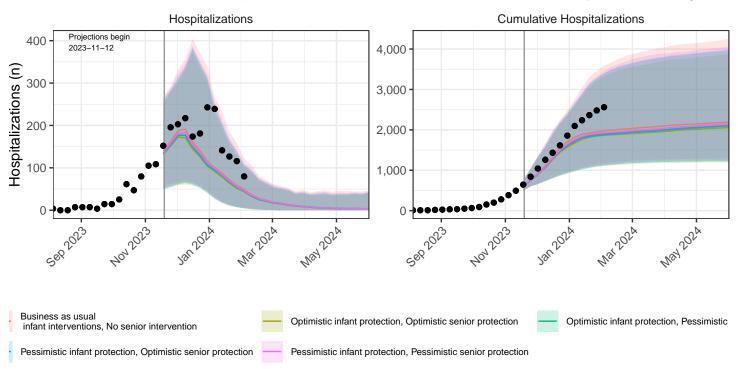
California, Ensemble projections for incident and cumulative hospitalizations by scenario, all ages.



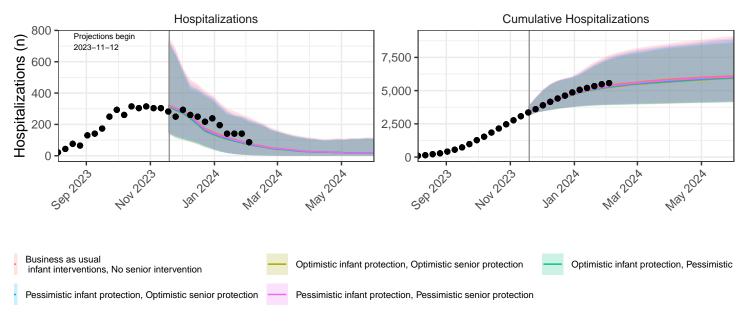
Colorado, Ensemble projections for incident and cumulative hospitalizations by scenario, all ages.



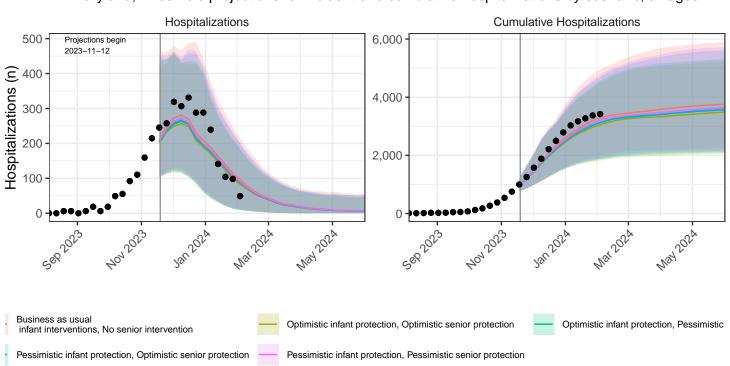
Connecticut, Ensemble projections for incident and cumulative hospitalizations by scenario, all ages.



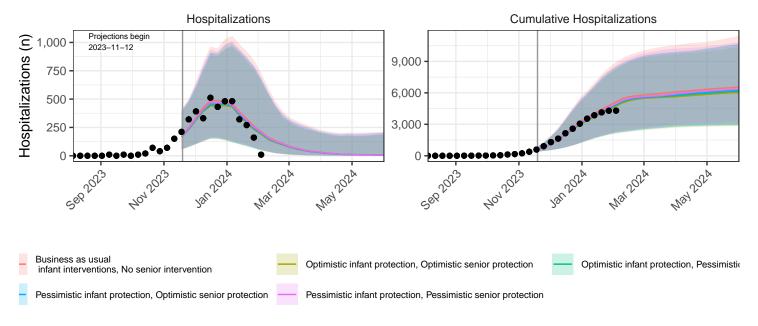
Georgia, Ensemble projections for incident and cumulative hospitalizations by scenario, all ages.



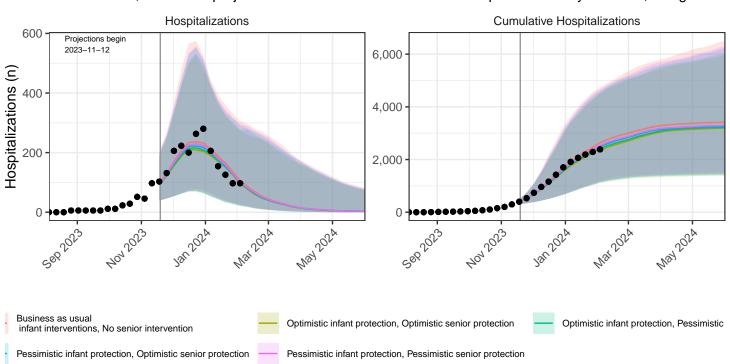
Maryland, Ensemble projections for incident and cumulative hospitalizations by scenario, all ages.



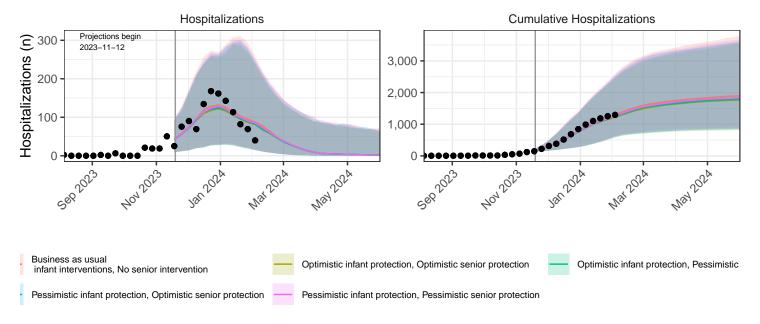
Michigan, Ensemble projections for incident and cumulative hospitalizations by scenario, all ages.



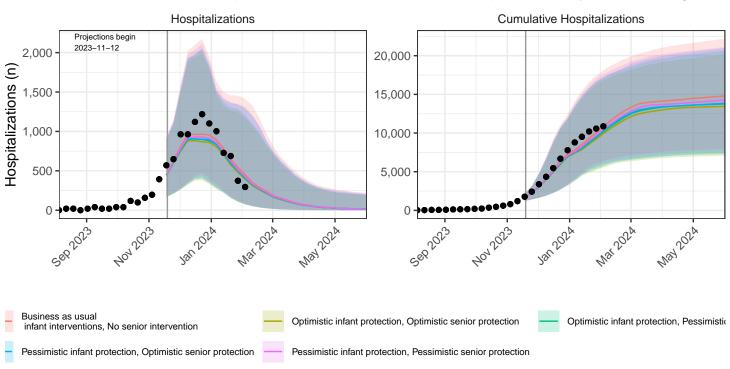
Minnesota, Ensemble projections for incident and cumulative hospitalizations by scenario, all ages.



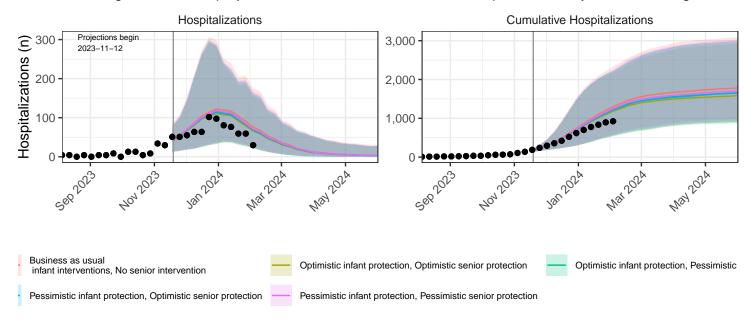
New Mexico, Ensemble projections for incident and cumulative hospitalizations by scenario, all ages.



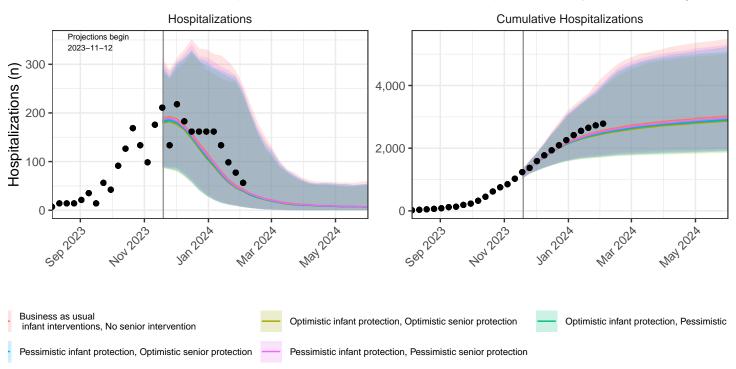
New York, Ensemble projections for incident and cumulative hospitalizations by scenario, all ages.



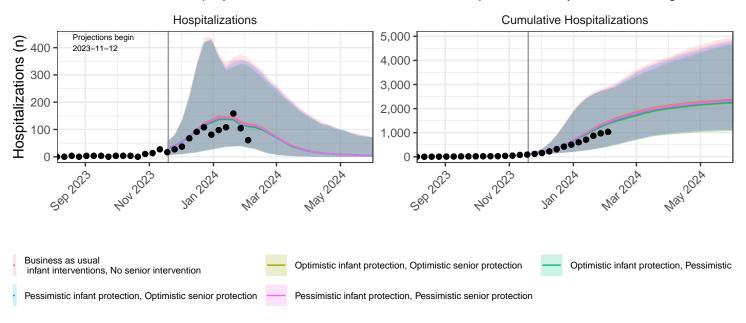
Oregon, Ensemble projections for incident and cumulative hospitalizations by scenario, all ages.



Tennessee, Ensemble projections for incident and cumulative hospitalizations by scenario, all ages.



Utah, Ensemble projections for incident and cumulative hospitalizations by scenario, all ages.



State Scenario Comparisons by Age

The scenario projections by age group were also very similar between scenarios within each state, with increased peak and cumulative size as scenarios became more pessimistic. The state projections also follow the empirical age-specific hospitalizations well for the younger age groups, however, as with the national projections, there is significant under-projection of hospitalizations in the 65-130 year age group, though the 95% projection intervals of the cumulative do contain the empirical data. This age group also substantially exceeded both peak and cumulative hospitalizations from the 2022-23 season, which was considered substantially larger; this may indicate a change in testing or reporting among this age group, and not a difference in infection or disease. Horizontal lines are given for prior peak incident and cumulative hospitalizations from the 2022-23 season, taken from RSV-NET (which is used as a proxy for hospitalizations). Lines represent the median ensemble projections, and shaded regions represent the 95% prediction intervals.

United States, Ensemble projections of incident and cumulative RSV hospitalizations, by Age

