

COVID-19 Vaccination of Individuals Aged 65 Years and Over in France: Clinical and Economic Impact of Vaccine Choice

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BACKGROUND

- In France, mRNA vaccines against COVID-19 are preferentially recommended for those at highest risk of severe illness from COVID-19, including adults aged ≥65 years, who were targeted by the autumn 2023 vaccination campaign¹
- BNT162b2 vaccine was the only mRNA vaccine available during this campaign, similarly to autumn 2024 campaign
- The vaccination coverage was estimated at 30.2% among French adults aged ≥65 years²
- The elderly population accounted for 63% of COVID-19 cases admitted to intensive care during the 2023-2024 vaccination season in France²
- A recent systematic review and meta-analysis in older adults aged ≥50 years by Kavikondala that included 24 observational studies found a significantly lower risk of infections (including symptomatic and severe infections, risk ratio [RR] for infection, 0.72; 95% CI, 0.64-0.80) and hospitalization (RR, 0.65; 95% CI, 0.53-0.79) associated with the mRNA-1273 vaccine compared to the BNT162b2 vaccine. The observed results were consistent in a subgroup of patients aged ≥65 years³

OBJECTIVE

- The aim of this study was to retrospectively evaluate the public health and economic impact of COVID-19 vaccination for individuals aged ≥65 years, comparing the mRNA-1273 variant-updated vaccine (XBB.1.5) against the BNT162b2 variant-updated vaccine (XBB.1.5) over a 1-year analytic time horizon (October 2023-September 2024) in France

METHODS

Study Design

- A previously developed Susceptible-Exposed-Infected-Recovered (SEIR) dynamic transmission model and infection consequences decision tree was adapted to France for this analysis.⁴ This model was assessed by the French HTA agency (HAS CEESP), which did not raise any major reservation on its methodology⁵
- The SEIR model was used to predict the total number of SARS-CoV-2 infections (ie, asymptomatic and symptomatic) during the analytic time horizon (Figure 1)
- The number of symptomatic infections, COVID-19-related hospitalizations and deaths, and associated quality-adjusted-life years lost and costs were predicted using a decision tree for each vaccination strategy (Figure 2)
- Two vaccination strategies (the mRNA-1273 variant-updated vaccine and the BNT162b2 variant-updated vaccine) were assessed, targeting individuals aged ≥65 years using the 30.2% vaccination coverage estimated in autumn 2023 by Santé Publique France, with vaccination starting in October 2023

Figure 1. Dynamic transmission model structure

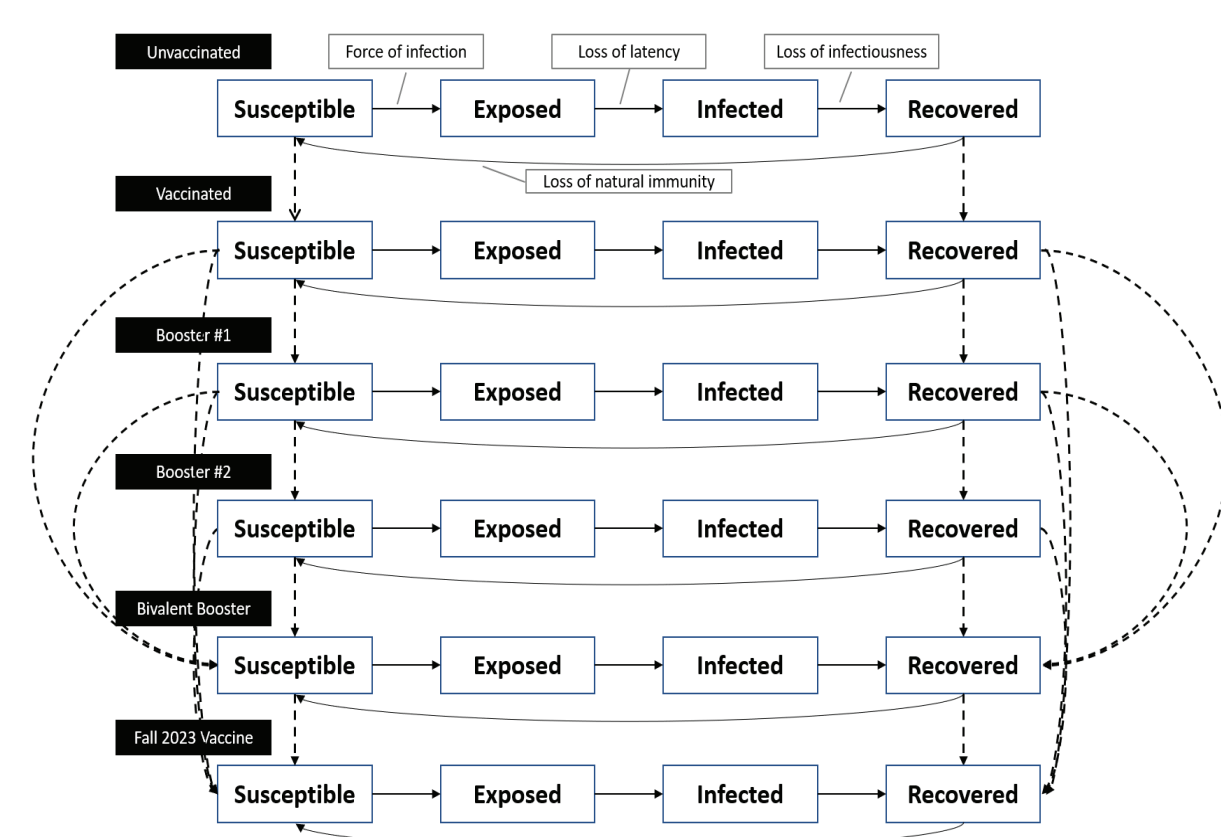
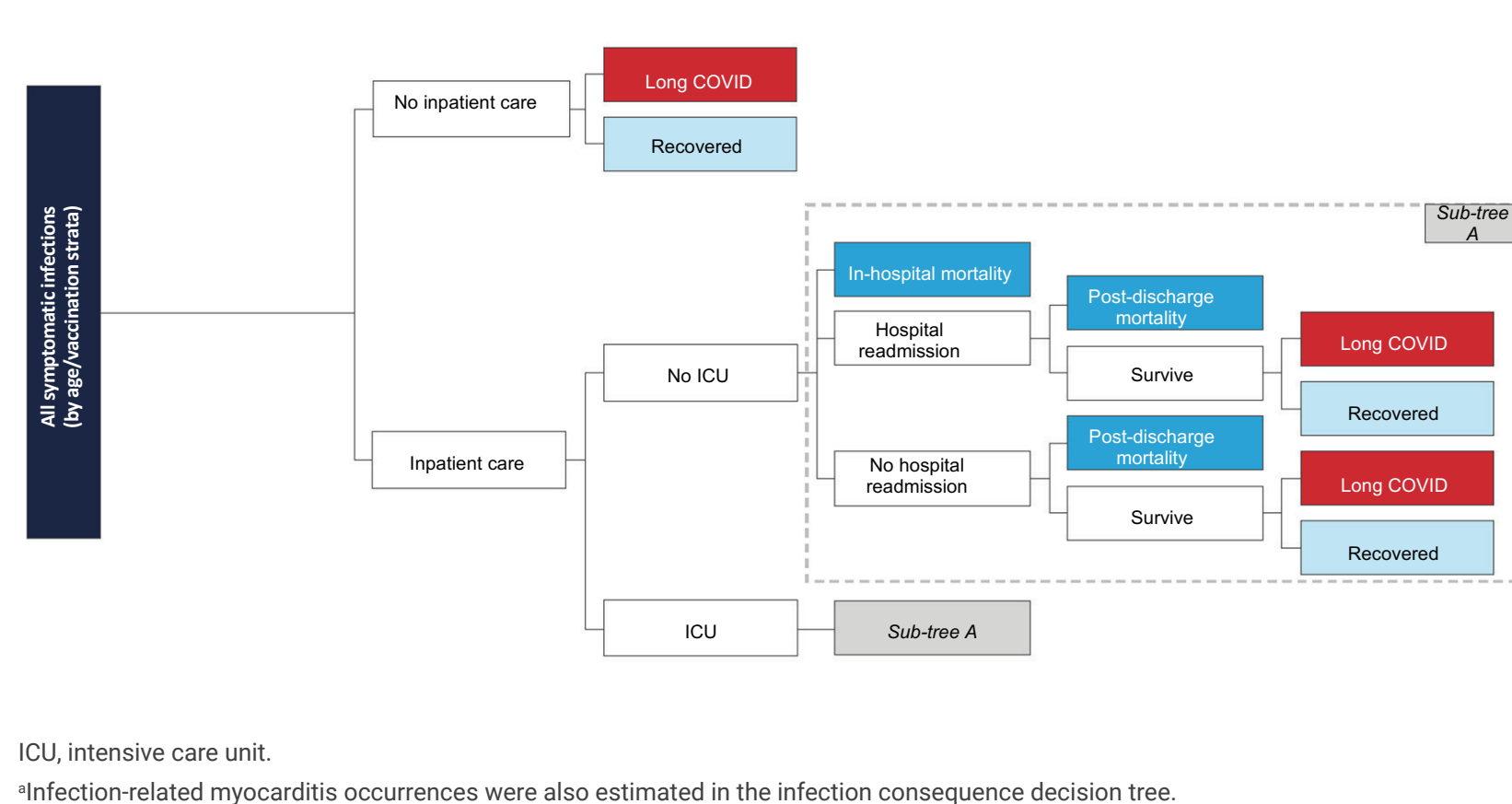


Figure 2. Infection consequence decision tree structure^a



ICU, intensive care unit.
^aInfection-related myocarditis occurrences were also estimated in the infection consequence decision tree.

Model Inputs

- The SEIR model was calibrated to reproduce the number of COVID-related hospitalizations in France, informed by national surveillance reports (Santé Publique France) for the time period between October 2023 and January 2024⁶
 - At the time of the analysis, due to the lack of published data, the number of hospitalizations from February 2024 to September 2024 used for model calibration was assumed to be half of the number of hospitalizations reported by Santé Publique France in the prior year
- The model takes into account residual protection from previous vaccination, natural infection, and the predicted effectiveness against infection and hospitalization of the autumn 2023 vaccines
- The model requires absolute vaccine efficacy (VE) inputs, as it is structured to compare the vaccinated strata to the unvaccinated model strata (ie, having not received any COVID-19 vaccination before)
 - As VE data against hospitalization and infection for absolute effectiveness of the mRNA-1273 XBB.1.5 monovalent vaccine were not available, real-world data on the mRNA-1273 bivalent BA.4/BA.5 variant vaccine (mRNA-1273.222) were used for VE against hospitalization (retrieved from a prospective study by Tseng et al. (2023))⁷
 - VE against infection was retrieved from the meta-analysis conducted by Pratama et al. (2022), which estimated the VE of the original mRNA-1273 monovalent booster against BA1/BA.2⁸
- The RRs for infection (0.74; 95% CI, 0.62-0.88) and hospitalization (0.69; 95% CI, 0.53-0.89) estimated in the Kavikondala meta-analysis for individuals aged ≥65 years were used to calculate VEs for the updated BNT162b2 vaccine
- Waning of both vaccines boosters were assumed to be the same as monovalent vaccines against Omicron BA.1/BA.2 and were obtained from a meta-analysis by Higdon et al. (2022).⁹ VE input values and waning rates are summarized in Table 1
- Rates of symptomatic COVID-19 infections, hospitalizations, and hospital deaths varied by age group (Table 2)
- Long COVID prevalence (8%) among infected individuals was informed from a French survey conducted by Santé Publique France¹⁰
- The unit cost for the mRNA-1273 variant-updated vaccine and the BNT162b2 variant-updated vaccine was assumed to be equivalent
- Other input parameters were based on French-specific data, when available, and other relevant literature
- Sensitivity analyses assessed the robustness of specific parameter estimates; where 95% confidence intervals were not available, parameters were varied by ± 25%

Table 1. Vaccine Effectiveness and Waning^a Assumptions in Patients Aged ≥65 Years

		mRNA-1273 variant-updated vaccine	BNT162b2 variant-updated vaccine
Infection	VE	57.1%	42.1%
	Waning	4.8%	4.8%
Hospitalization	VE	84.3%	77.2%
	Waning	1.4%	1.4%

^aWaning rate per month.

Table 2. Clinical Model Parameters per Age Group

	Proportion of infections with symptoms ^a	Probability of hospitalization given symptomatic infection ^b (95% CI)	Hospital death ^b (95% CI)	Post-discharge mortality ^c (95% CI)
Age group, %				
65-69 years	63.5	9.6 (7.8-11.6)	12.3 (10.0-14.8)	2.7 (0.0-8.4)
70-79 years	63.5	9.6 (7.8-11.6)	12.3 (10.0-14.8)	
≥80 years	92.1	27.4 (22.2-32.9)	15.4 (12.5-18.5)	

CI, confidence interval.
^aEstimated from model calibration. ^bDirectorate of Research, Studies, Evaluation, and Statistics (DREES): COVID-19: results by age from linkage between SI-VIC, SI-DEP, and VAC-SI. ^cRamzi ZS. Hospital readmissions and post-discharge all-cause mortality in COVID-19 recovered patients: a systematic review and meta-analysis. *Am J Emerg Med*. 2022;51:267-279.

CONCLUSIONS

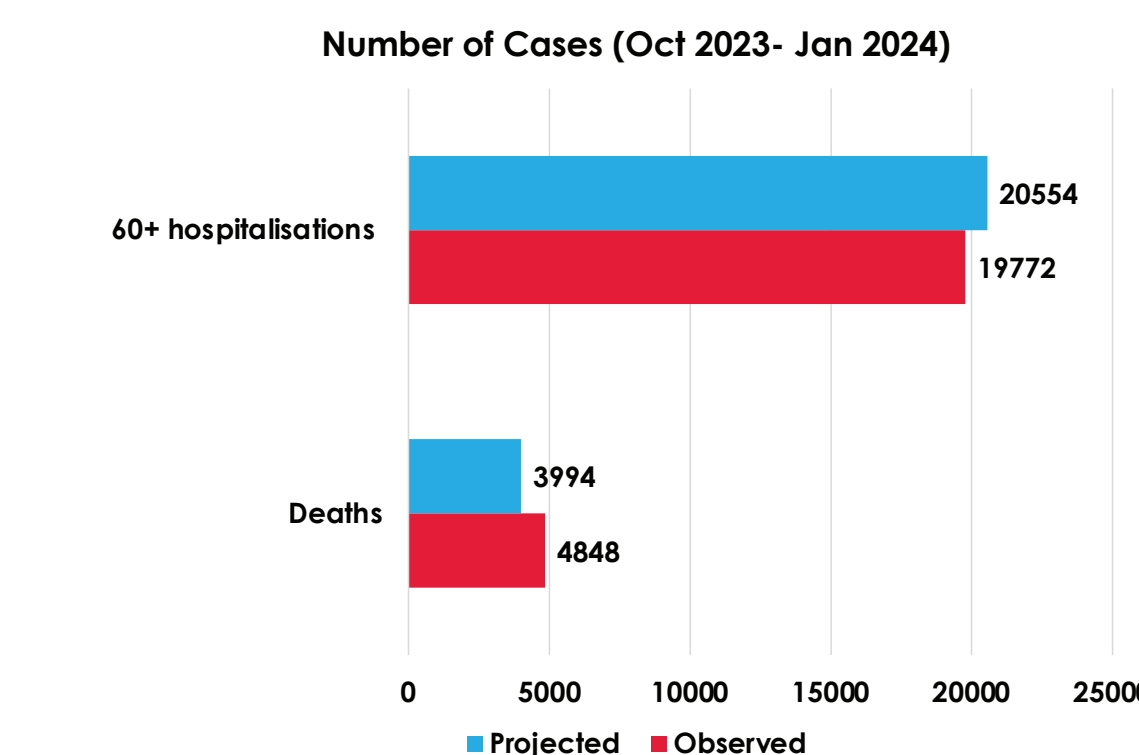
- Vaccinating the French population aged ≥65 years with the updated mRNA-1273 vaccine in autumn 2023 would have prevented 2660 hospitalizations, 400 deaths, and 3819 long COVID cases related to COVID-19 and would have generated incremental economic savings compared with vaccination with the updated BNT162b2 vaccine
- Further efforts to improve vaccine access and uptake in vulnerable populations such as older adults are essential to ensure a substantial long-term decrease in the burden of COVID-19 on individuals and the healthcare system

RESULTS

Calibration Results

- Model projections over the analytic period showed a <4% difference with the observed number of hospitalizations reported by Santé Publique France between October 2023 and January 2024 (Figure 3)

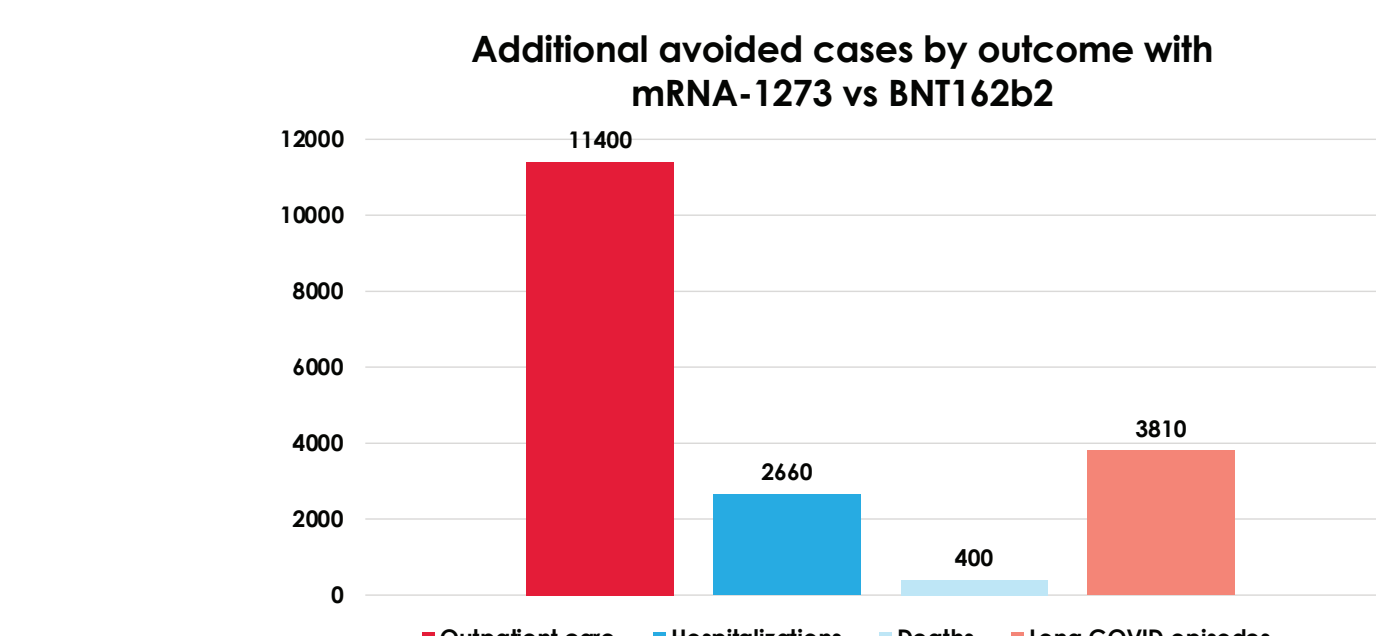
Figure 3. Model projections vs epidemiological targets (October 2023-January 2024)



Public Health Impact of mRNA-1273 Vaccination vs BNT162b2 Vaccination in Adults Aged ≥65 Years

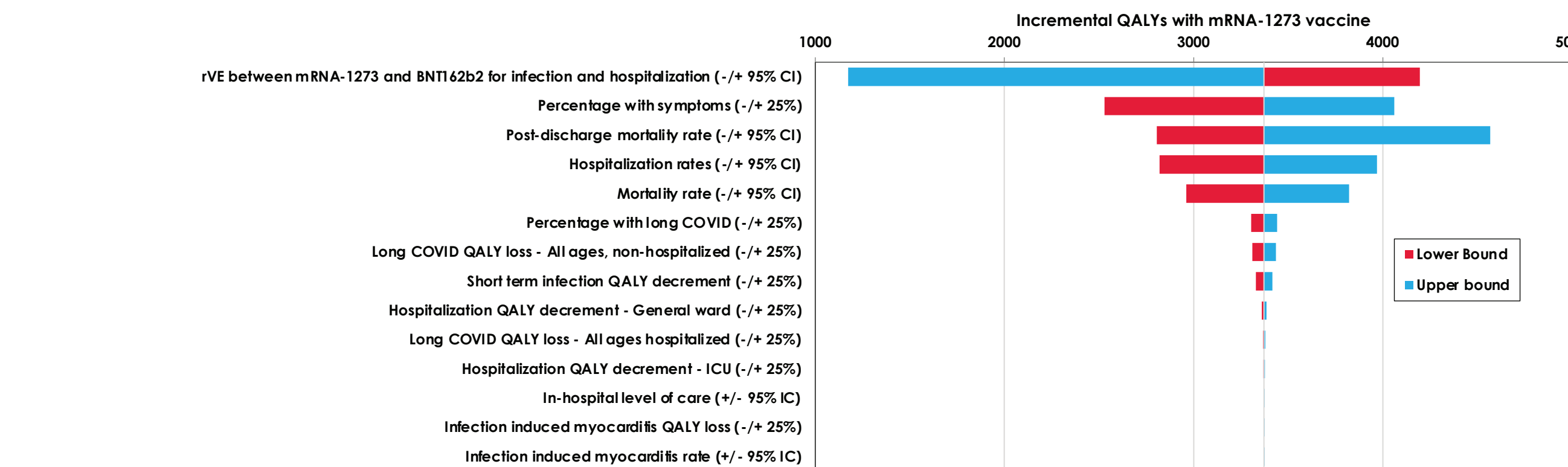
- With identical vaccine coverage of 30.2%, compared to the BNT162b2 vaccine, vaccination targeting those aged ≥65 years with the mRNA-1273 vaccine during the autumn 2023 campaign would have prevented an additional 2660 hospitalizations, 3810 cases of long COVID, and 400 deaths (Figure 4), corresponding to 3372 quality-adjusted life-years gained

Figure 4. Clinical outcomes in the population aged ≥65 years vaccinated with the mRNA-1273 vaccine vs the BNT162b2 vaccine



- For a BNT162b2 vaccine program to achieve the same healthcare treatment costs as an mRNA-1273 vaccine program, an **absolute 14 percentage points** increase in vaccination coverage rate would be needed
- Based on the deterministic sensitivity analyses, the incremental quality-adjusted life-years gained with the use of the mRNA-1273 vaccine ranged between 1174 and 4569 (Figure 5)

Figure 5. Deterministic sensitivity analyses of incremental QALYs in the population aged ≥65 years vaccinated with the mRNA-1273 vaccine vs the BNT162b2 vaccine

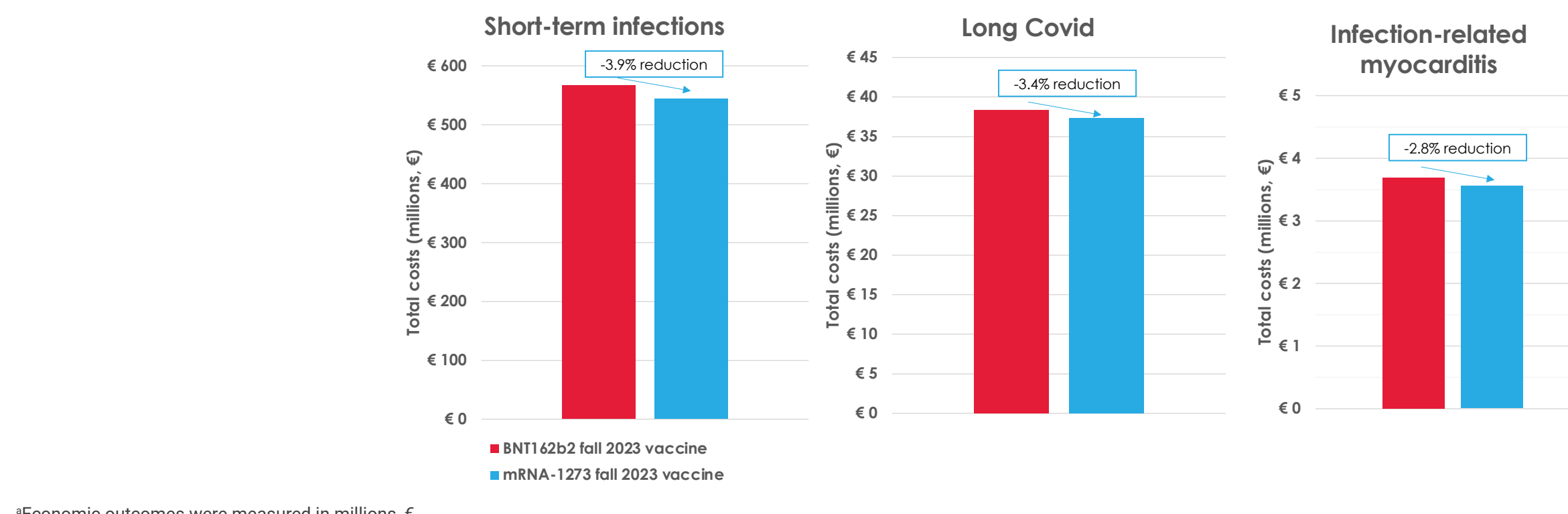


CI, confidence interval; QALY, quality-adjusted life-year; rVE, relative vaccine efficacy.

Economic Impact of mRNA-1273 Vaccination vs BNT162b2 Vaccination in Adults Aged ≥65 Years

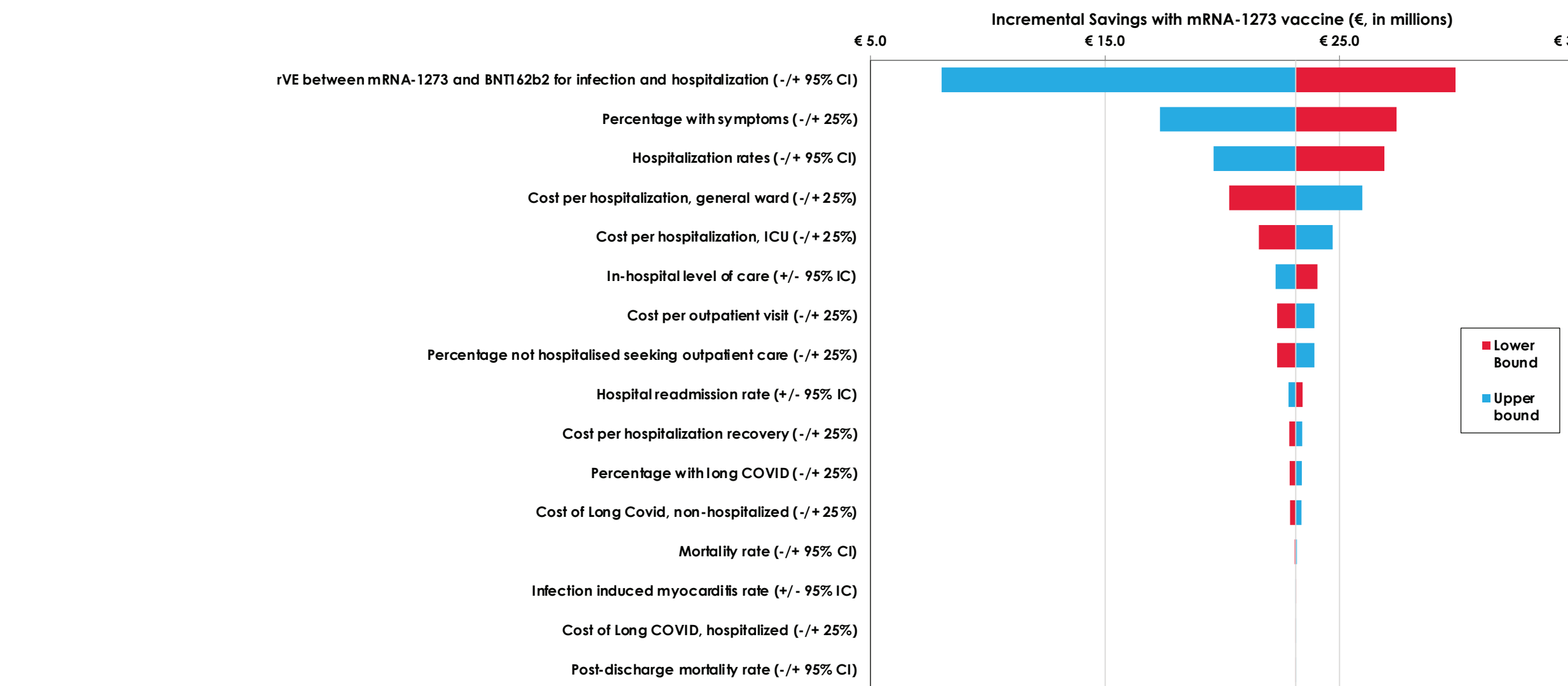
- Total costs associated with short-term infection, long COVID, and infection-related myocarditis were lower in individuals aged ≥65 years who received the variant-updated mRNA-1273 compared with those who received the BNT162b2 variant-updated vaccine (Figure 6)
- The public health impact of mRNA-1273 vaccination translated into an economic savings of €23 million in saved direct COVID-19 treatment costs for the French healthcare system compared with BNT162b2 vaccination
- Based on the deterministic sensitivity analyses, the incremental savings with the use of the mRNA-1273 vaccine ranged between €8 million and €30 million (Figure 7)

Figure 6. Economics outcomes^a in individuals aged ≥65 years vaccinated with the mRNA-1273 autumn vaccine or the BNT162b2 autumn 2023 vaccine



^aEconomic outcomes were measured in millions, €.

Figure 7. Deterministic sensitivity analyses of incremental savings in the population aged ≥65 years vaccinated with the mRNA-1273 vaccine vs the BNT162b2 vaccine



CI, confidence interval; ICU, intensive care unit; rVE, relative vaccine efficacy.

LIMITATIONS

- One study limitation is that at time of the analysis, the model calibration could not include hospitalizations reported in France for the entire period (October 2023-September 2024); thus, an update of this analysis considering all published data for this period is needed
- Use of 2023/2024 season data may limit findings due to uncertainties in the epidemiology of COVID-19, vaccine uptake, vaccine effectiveness for future seasons

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Disclosures

NEM, MU, CD, KJ, EB, and AC are employees of Moderna, Inc., and hold stock/stock options. MK is a shareholder in Quadrant Health Economics, Inc., which was contracted by Moderna, Inc., to conduct this study. AL and MM are consultants at Quadrant Health Economics, Inc.

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