Comparison of the Clinical and Economic Impact of Two COVID-19 mRNA Vaccines in High Risk Individuals in the Tokyo Prefecture

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BACKGROUND

- In Japan, messenger RNA (mRNA)-based vaccines against SARS-CoV-2 infection have been effective in preventing symptomatic disease¹
- Immunocompromised individuals and those aged ≥65 years are considered to be at high risk of severe COVID-19 disease,² and updated COVID-19 vaccination may be beneficial for these populations
- A recent meta-analysis³ and study⁴ found that previously approved formulations of mRNA-1273 (Spikevax; Moderna, Inc., Cambridge, MA, USA) were more effective than BNT162b2 (Comirnaty; Pfizer Inc., New York, NY, USA) in preventing severe COVID-19 outcomes and hospitalization in immunocompromised populations and in older adults (≥65 years) in the United States, respectively
- Evaluating the effectiveness of the Moderna mRNA-1273 and Pfizer-BioNTech BNT162b2 Fall 2023 vaccines updated to target the XBB.1.5 variant in Tokyo (Japan) can inform prefecture-level vaccination strategies

OBJECTIVE

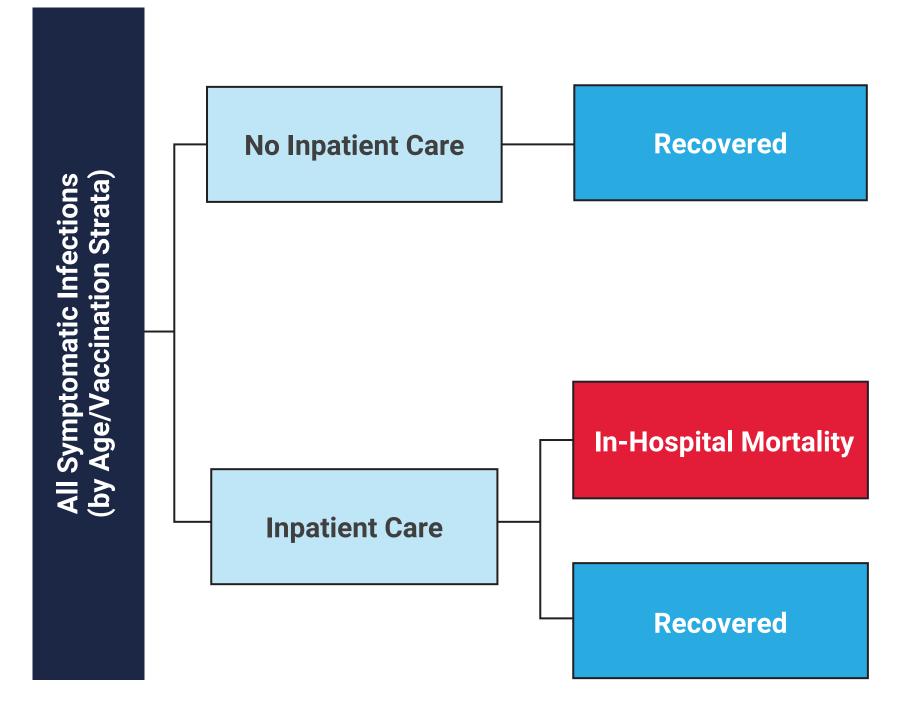
To estimate the impact of VE on clinical outcomes and treatment costs for the Moderna Fall 2023 updated COVID-19 mRNA vaccine (Moderna Fall 2023 vaccine) versus the Pfizer-BioNTech Fall 2023 updated COVID-19 vaccine (Pfizer BioNTech Fall 2023 vaccine) over a 1-year time horizon in the Tokyo prefecture in: 1) older adults (≥65 years) and 2) immunocompromised adults

METHODS

Model Overview

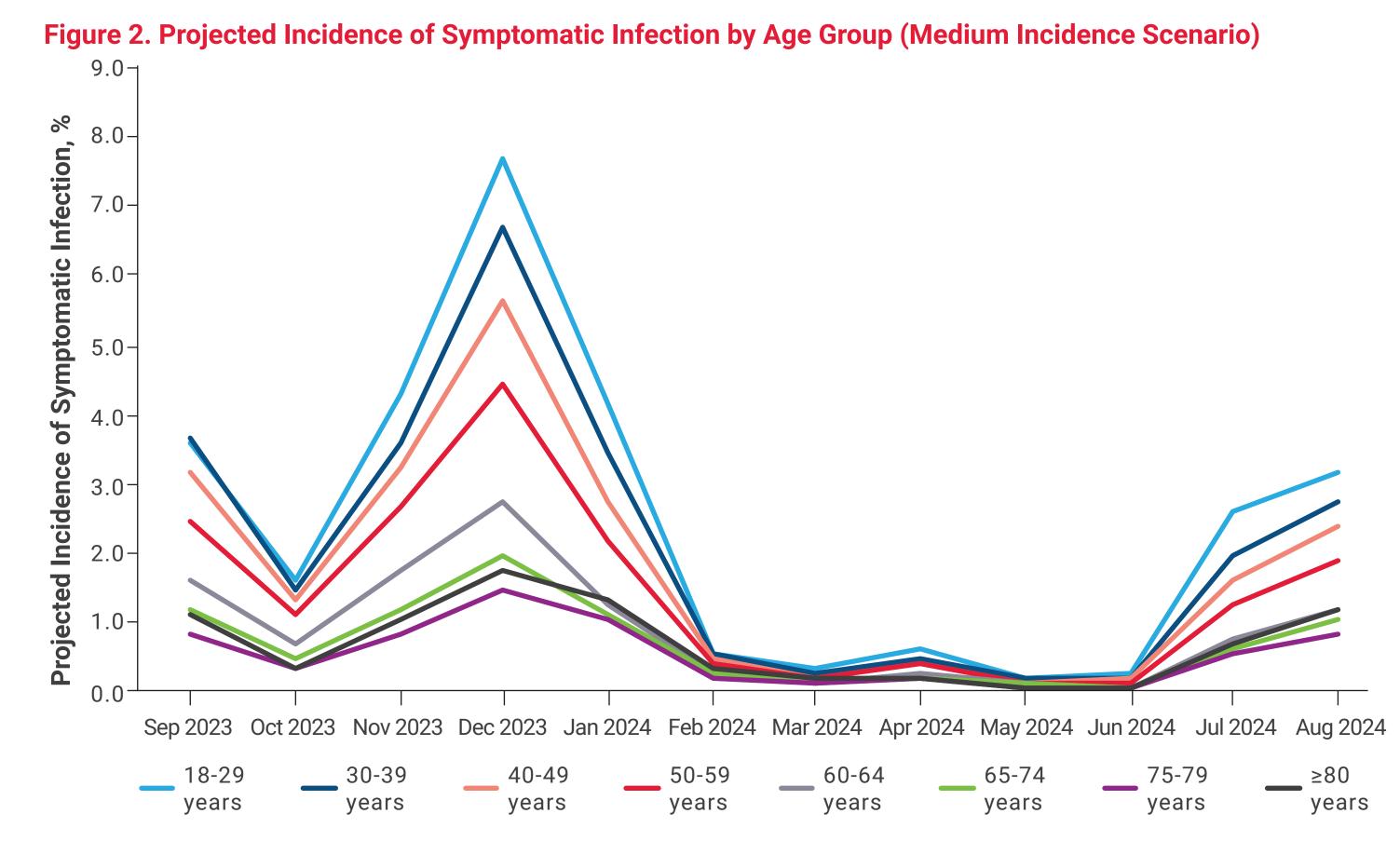
- A static decision-analytic model was used to estimate the clinical and economic outcomes between September 2023 and August 2024
- A simple Markov model with tunnel states was used to track the vaccination status through monthly cycles
- Individuals who developed medically attended symptomatic SARS-CoV-2 infection entered an infection consequences decision tree (Figure 1)
- The following consequences of SARS-CoV-2 infection were calculated in the model: medically attended symptomatic infections, hospitalizations, death, long COVID cases, and COVID-19 treatment costs

Figure 1. Infection Consequence Decision Tree



Model Inputs: Population Size and COVID-19 Incidence

- Assumptions for population size and COVID-19 incidence for both target populations are described in the Supplementary Methods (accessible through the QR code)
- The model considered the incidence of symptomatic COVID-19 by age (Figure 2)
 - Medium scenario incidence rates (base case) were derived from infection counts from the Tokyo prefecture between June 2022 and May 2023⁵
 - High and low incidence rates were set to 25% above and below the medium incidence scenario, respectively



Model Inputs: COVID-19-Associated Outcomes and Vaccine Coverage

- Base-case input probabilities of infection-related myocarditis, infection-related hospitalization, and mortality are provided in **Supplementary Table 1** (accessible through the QR code)
- Vaccine coverage for Fall 2023 was estimated from previous vaccination campaigns^{6,7} (Supplementary Figure 1, accessible through the QR code)

Model Inputs: VE of Moderna and Pfizer-BioNTech Fall 2023 Vaccines

- The Moderna and Pfizer-BioNTech Fall 2023 vaccines were assumed to be well matched against the current variant; VE was approximated by assuming the same VE of bivalent vaccines against BA.4/BA.5 (**Table 1**)
- VE against infection and hospitalization for adults aged ≥65 years and ≥18 years for the Moderna bivalent vaccine were obtained from the VERSUS study, a multicenter surveillance study in Japan⁸
- In immunocompromised individuals, the VE of the Moderna Fall 2023 vaccine was adjusted down by using data on the relative risk (RR) of hospitalizations in the immunocompromised compared to the general population9
- As there were no data on the RR of infection, VE was assumed to be the same as the general population9
- The VE of the Pfizer-BioNTech Fall 2023 vaccine was approximated by using the relative VE (rVE) between the bivalent vaccines in those aged ≥65 years⁴ and for immunocompromised individuals³

Table 1. VE and Monthly Waning Inputs

Outcome	VE (%)	Monthly Waning ^a (%)	
	Adults ≥65 years		
Infection			
Moderna Fall 2023 vaccine ⁸	75.2	1.4	
Pfizer-BioNTech Fall 2023 vaccine4	72.2	1.4	
Hospitalization			
Moderna Fall 2023 vaccine ⁸	84.9	4.8	
Pfizer-BioNTech Fall 2023 vaccine4	82.5	4.8	
Immuno	compromised adults (18-64 yea	ars)	
Infection			
Moderna Fall 2023 vaccine ⁹	54.7	1.4	
Pfizer-BioNTech Fall 2023 vaccine ³	46.7	1.4	
Immune	ocompromised adults (≥65 year	rs)	
Infection			
Moderna Fall 2023 vaccine ⁹	75.2	1.4	
Pfizer-BioNTech Fall 2023 vaccine ³	70.8	1.4	
Immune	ocompromised adults (≥18 year	rs)	
Hospitalization			
Moderna Fall 2023 vaccine ⁹	Fall 2023 vaccine ⁹ 63.1 4.8		
Pfizer-BioNTech Fall 2023 vaccine ³	58.1	4.8	

^aAssumed to be same as monovalent booster waning against the omicron variant.¹

Model Inputs: Cost and Resource Use

Base-case inputs for cost and resource use are summarized in Supplementary Table 2, accessible through the QR code

RESULTS

- In both the population aged ≥65 years and the immunocompromised population, the use of the Moderna Fall 2023. vaccine was predicted to prevent more COVID-19-related infections, hospitalizations, deaths, and long COVID cases compared with the Pfizer-BioNTech Fall 2023 vaccine for all incidence and rVE scenarios (Table 2)
- This reduced morbidity was projected to save ¥1372 million in treatment costs for those aged ≥65 years and ¥372 million for the immunocompromised population using the medium incidence scenario with base-case rVE (Table 2)

Table 2. Cases Prevented and Treatment Cost Savings of the Moderna Fall 2023 Vaccine Versus the Pfizer-BioNTech Fall 2023 Vaccine in Tokyo

Incidence Scenario	Symptomatic Infections (n)	Hospitalizations (n)	Deaths (n)	Long COVID (n)	Costs (¥, million)
Adults ≥65 years					
Low	4103	1151	137	874	1029
Medium	5471	1535	182	1165	1372
High	6839	1919	228	1457	1715
Medium (low CI for rVE)	4079	572	68	883	603
Medium (high CI for rVE)	6883	2583	307	1450	2204
Immunocompromised adul	lts (≥18 years)				
Low	1644	280	37	2	279
Medium	2192	373	50	570	372
High	2740	467	62	713	465
Medium (low CI for rVE)	4140	728	97	1076	720
Medium (high CI for rVE)	384	85	11	99	79

CONCLUSIONS

- Vaccinating adults aged ≥65 years and individuals who are immunocompromised with the Moderna Fall 2023 vaccine could prevent more COVID-19-related infections, hospitalizations, deaths, and long COVID cases, and reduce the associated treatment costs in Tokyo compared with the Pfizer-BioNTech Fall 2023 vaccine
- The comparative effectiveness of the updated Fall 2023 mRNA COVID-19 vaccines is based on observations of past formulations of these vaccines
 - Current assumptions were based on studies of previously approved formulations of mRNA-1273 and BNT162b2
- Continued study of the clinical outcomes of VE for 2023–2024 is required to determine the comparative VE and validate these modeled projections

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CI, confidence interval; rVE, relative vaccine effectiveness

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MK is a shareholder in Quadrant Health Economics Inc., which was hired by Moderna, Inc., to conduct this analysis. MM and AL are consultants to Quadrant Health Economics Inc. Al has received honoraria from Moderna Japan Inc., Pfizer Japan Inc., Shionogi Co Ltd., Takeda Pharmaceutical Co Ltd., and AstraZeneca Japan Inc. YH, KJ, NVdV, and EB are employees of Moderna, Inc., and may hold stock/stock options in the company.



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