Cost-Effectiveness Analysis of Nuvaxovid® Vaccination for Japanese Elderly Population

SUPPREMENTAL MATERIAL

Table S1. Model parameters

Item			Value	Settings in DSA			Settings in PSA			Source
				Lower limit	Upper limit	Range	Distribution	Parameters[a]		
VE of NVX-CoV2373 vaccine (%)										
Analysis population 1	Against infection	NVX-CoV2373 primary vaccinations	88.9	20.2	99.7	95% CI	Beta (SE 10%)	10.21	1.27	[3] (aged ≥65 years)
		NVX-CoV2373 booster vaccination	88.9	20.2	99.7	95% CI	Beta (SE 10%)	10.21	1.27	
	Against severe disease	NVX-CoV2373 primary vaccinations	86.9	73.7	93.5	95% CI	Beta (SE 10%)	12.23	1.84	
		NVX-CoV2373 booster vaccination	86.9	73.7	93.5	95% CI	Beta (SE 10%)	12.23	1.84	
Analysis population 2	Against infection	NVX-CoV2373 booster vaccination	88.9	20.2	99.7	95% CI	Beta (SE 10%)	10.21	1.27	
	Against severe disease	NVX-CoV2373 booster vaccination	86.9	73.7	93.5	95% CI	Beta (SE 10%)	12.23	1.84	
VE of COVID-19 mRNA vaccine (%)										
Analysis population 2	Against infection	No booster vaccination[b]	50.6	14.4	71.5	95% CI	Beta (SE 10%)	48.89	47.73	[4]
	Against severe disease	No booster vaccination[b]	83.4	66.7	100.0	±20%	Beta (SE 10%)	15.77	3.14	[5, 6]
Incidence of COVID-19 (per 100,000 person-days)										

Item		Value	Settings in DSA			Settings in PSA			Source
			Lower limit	Upper limit	Range	Distribution	Parameters[a]		
Analysis population 1	No vaccination	71.5	57.2	85.8	±20%	Triangular[c]	Min: 13.53 Max: 175.71	Mode: 71.53	[4, 7, 10, 11]
	NVX-CoV2373 primary and booster vaccinations[d]	7.94	-	-	-	-	-	-	[11], [3] (aged ≥65 years)
Analysis population 2	No booster vaccination[d]	35.3	-	-	-	-	-	-	[4, 11]
	NVX-CoV2373 booster vaccination[d]	7.94	-	-	-	-	-	-	[11], [3] (aged ≥65 years)
Distribution of clinical outcomes (%)									
No vaccination	Asymptomatic infection	35.6	-	-	-	Dirichlet	0.36	-	[12]
	Mild disease	49.5	-	-	-		0.50	-	-
	Moderate disease	9.4	-	-	-		0.09	-	[13]
	Severe disease	1.1	-	-	-		0.01	-	[14]
	Death	4.4	-	-	-		0.04	-	[14]
Duration of clinical stages (days)									
Incubation period		2.9	2.6	3.2	95% CI	Gamma	358.98	0.01	[15]
Asymptomatic infection		6.0	4.8	7.2	±20%	Gamma (SE 10%)	100	0.06	[2]
Mild disease	In mild state	11.0	10.9	11.1	95% CI	Gamma	21,040.90	0.001	Data are averages

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			Lower limit	Upper limit	Range	Distribution	Parameters[a]		
Moderate disease	In mild state	11.2	10.9	11.5	95% CI	Gamma	6970.60	0.002	calculated using the MDV claims database
	In moderate state	6.4	6.3	6.5	95% CI	Gamma	7190.70	0.001	
Severe disease	In mild state	6.9	6.3	7.5	95% CI	Gamma	591.33	0.012	
	In moderate state	2.6	2.2	3.0	95% CI	Gamma	183.43	0.014	
	In severe state	8.6	8.3	8.9	95% CI	Gamma	3886.45	0.002	
	In recovery state	5.7	4.6	6.8	±20%	Gamma (SE 10%)	100	0.06	[2]
Death[e]	In mild state	3.4	2.7	4.1	95% CI	Gamma	85.27	0.040	Data are averages calculated using the MDV claims database
	In moderate state	4.9	4.1	5.7	95% CI	Gamma	162.41	0.030	
	In severe state	8.7	7.8	9.6	95% CI	Gamma	391.32	0.022	
Incidence of long COVID (%)		40.1	34.7	45.5	95%CI	Beta	126.75	189.34	[16]
Duration of long COVID (days)		760.2 (108.6 weeks)	608.2	912.2	±20%	Log-normal (SE 10%)	6.63	0.01	[17]
Costs (JPY)									
Vaccination cost	NVX-CoV2373 vaccine price	9000	4500	13,500	±50%	Gamma (SE 10%)	100	90.00	Assumption for the analysis
	Vaccine administration	3700	2960	4440	±20%	Gamma (SE 10%)	100	37.00	[18]

Item				Value	Settings in DSA			Settings in PSA			Source
					Lower limit	Upper limit	Range	Distribution	Parameters[a]		
Treatment costs for COVID-19[f, g]	Recovered	Asymptomatic infection		0	-	-	-	-	-	-	
		Mild disease (JPY 93,242)	Outpatient expenses[h]	8035	6428	9642	±20%	Gamma (SE 10%)	100	80.35	
			Hospitalization expenses	804,361	795,547	813,175	95% CI	Gamma	31,992.95	25.14	
			Hospitalization rate (%)	10.7	8.6	12.8	±20%	Beta (SE 10%)	89.19	744.39	[19]
		Moderate disease		1,515,231	1,498,133	1,532,329	95% CI	Gamma	30,168.88	50.22	
		Severe disease		3,085,669	3,006,771	3,164,567	95% CI	Gamma	5875.90	525.14	
	Death	Severe disease		3,320,958	3,3037,040	3,604,876	95% CI	Gamma	525.60	6318.44	
Treatment cost for long COVID				17,640	14,112	21,168	±20%	Gamma (SE 10%)	100	176.40	[20]
Utilities											
Utility of COVID-19	Asymptomatic infection			0.8695	0.6956	1.0000	±20%	Beta (SE 10%)	12.18	1.83	[21]
	Mild disease			0.5095	0.4076	0.6114	±20%	Beta (SE 10%)	48.54	46.73	[17]
	Moderate disease			0.2895	0.2316	0.3474	±20%	Beta (SE 10%)	70.76	173.66	

Item		Value	Settings in DSA			Settings in PSA			Source
			Lower limit	Upper limit	Range	Distribution	Parameters[a]		
	Severe disease	0.0000	-	-	-	-	-	-	
	Recovered	0.5095	0.4076	0.6114	±20%	Beta (SE 10%)	48.54	46.73	Assumption
Disutility of long COVID		−0.1100	−0.1300	−0.0900	95% CI	Beta	103.32	835.92	[22]

CI: confidence interval; COVID-19: coronavirus disease 2019; DSA: deterministic sensitivity analysis; ICU: intensive care unit; JPY: Japanese yen; long COVID: long coronavirus disease; MDV: Medical Data Vision Company Limited; mRNA: messenger RNA; PSA: probabilistic sensitivity analysis; SE: standard error; VE: vaccine efficacy.

a Beta (α, β), triangular (min, max, mode), Dirichlet (α), gamma (α, β), log-normal (μ, σ).

b VE of COVID-19 mRNA vaccine 180 days after completing the second primary vaccination (individuals who had only received one vaccination were considered to have no immunity and, therefore, no VE).

c The minimum and maximum values during the evaluation period (July 2022 to October 2022) were set as parameters.

d Values were calculated using the equation: infection rate = Y × (1 − VE% against infection), with Y being the infection rate in unvaccinated individuals (i.e., 71.5 per 100,000 person-days). Ranges for the sensitivity analyses were calculated using the ranges provided for Y and the respective VEs.

e The duration of the clinical stages was assumed to be the same as for severe disease.

f Treatment costs from the onset of COVID-19 to recovery or death.

g Treatment costs were calculated by multiplying hospitalization charges by the number of days of the clinical stage. For moderate and severe disease, the cost of supplemental oxygen inhalation and of ICU admission and ventilation, respectively, were calculated during hospitalization. It was assumed that 10.7% of patients with mild cases would be hospitalized [11]. Outpatient visits and antigen test costs were calculated once for individuals who were not hospitalized. For the treatment of long COVID, it was assumed that individuals had one outpatient visit (consultation fee was JPY 735) per month for the duration of long COVID.

h Outpatient expenses were the sum of the consultation fee (JPY 735), the in-hospital triage fee (JPY 3,000) and the antigen test cost (JPY 4,300).

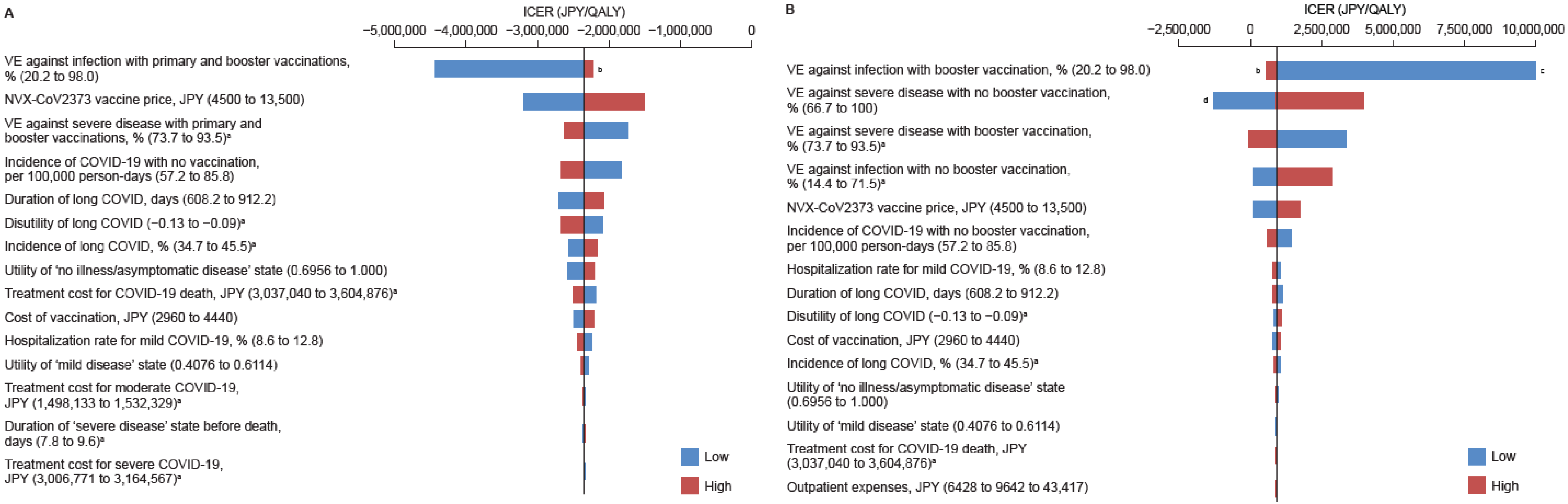
Table S2. Model parameters for scenario analysis, incorporation of productivity loss

Item		Value	Source
Productivity loss	Absence from work due to COVID-19 vaccination	0.5 day	Assumption
	Productivity loss due to COVID-19 [a]	2,280 JPY	[23, 24]

COVID-19: coronavirus disease 2019; JPY: Japanese yen

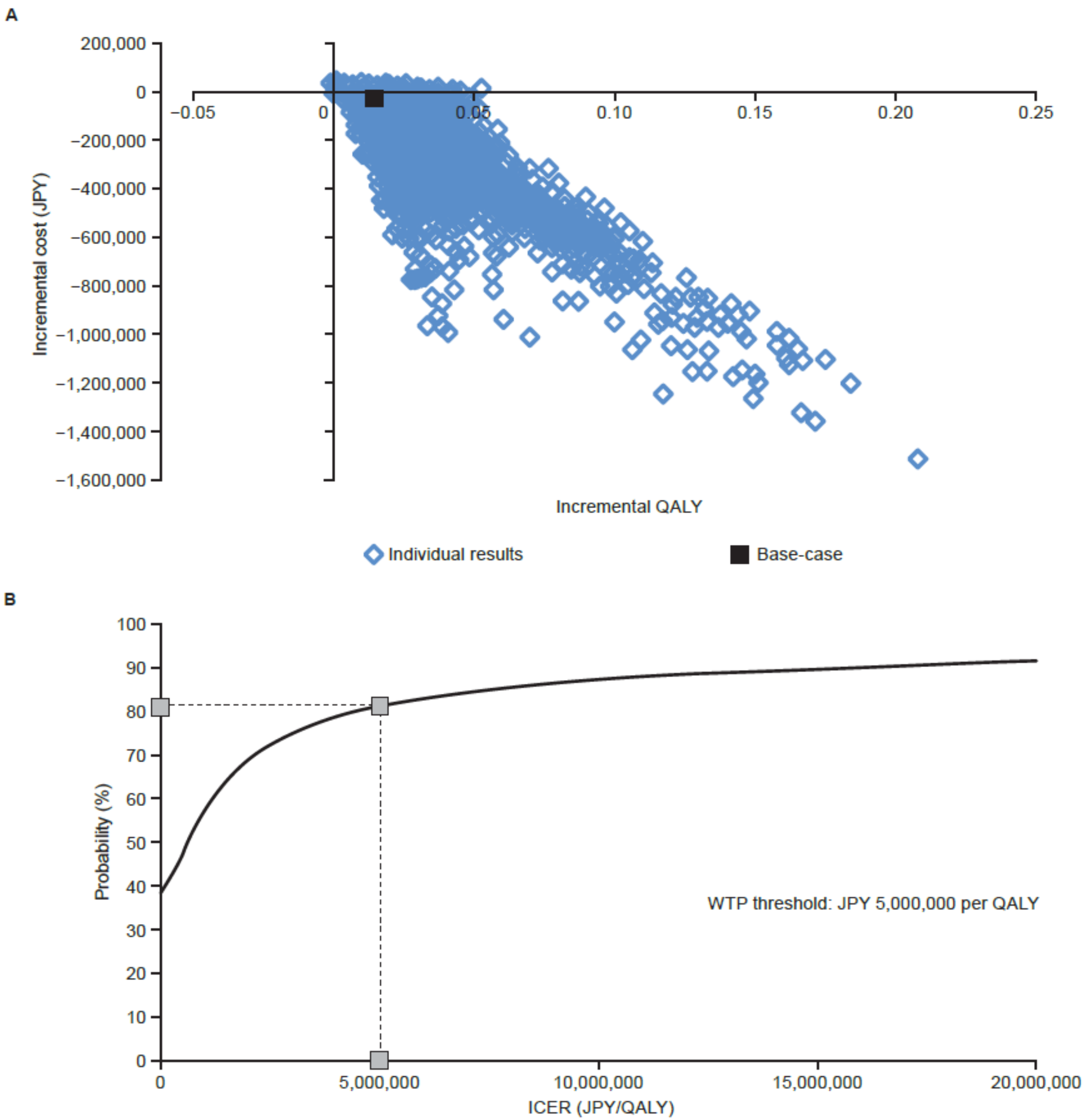
[a] Calculated using the employment rate of adults aged ≥65 years in Japan (25.4%), the proportion of regular employees (47.8%) and non-regular employees (44.7%), and the average wage in the target population (regular employees: JPY 11,222 per day; non-regular employees: JPY 8,074 per day).

Figure S1. Deterministic Sensitivity analysis



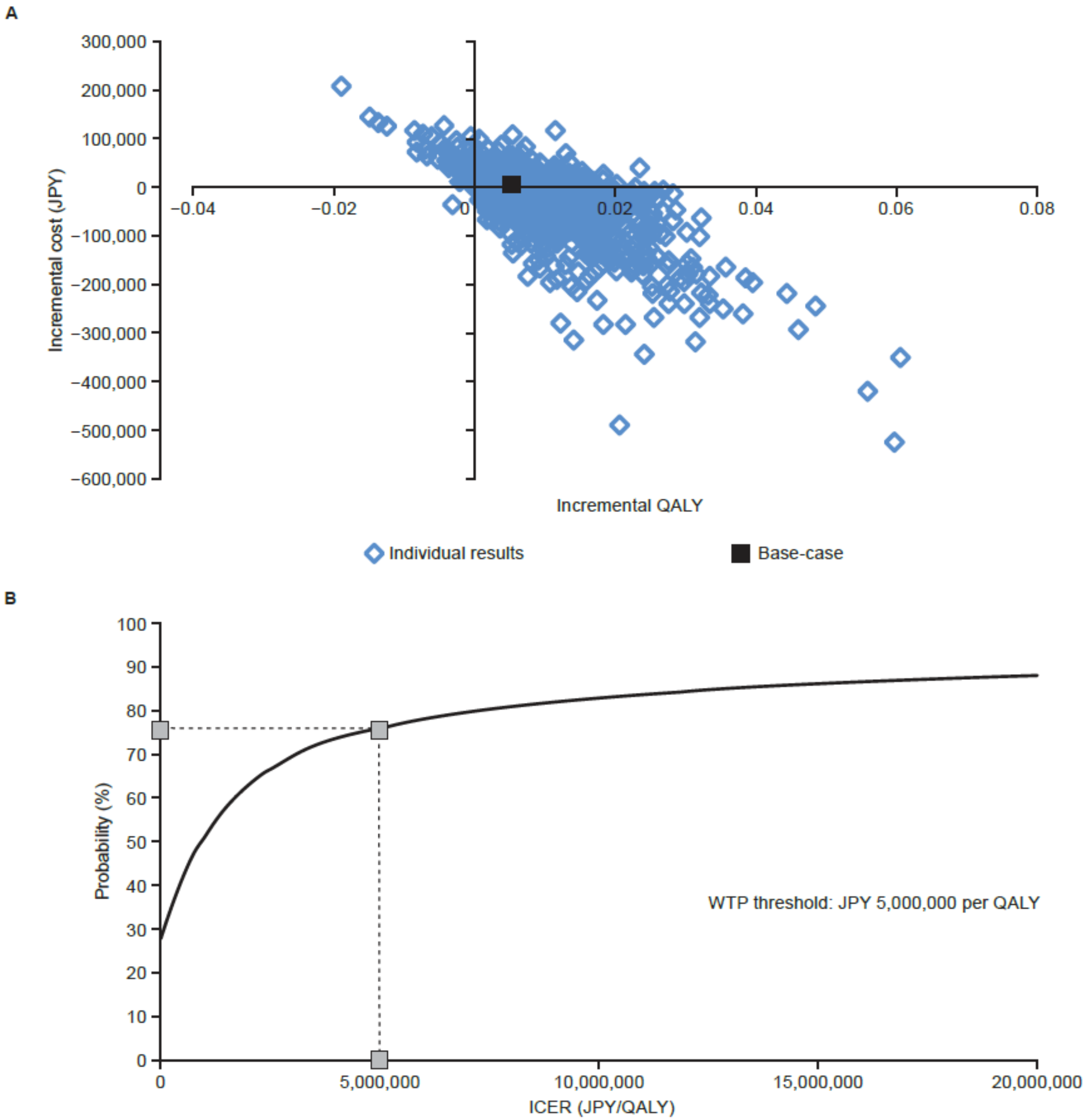
Tornado diagrams of deterministic sensitivity analyses showing the 15 variables with the largest impact on the ICER of (**A**) NVX-CoV2373 primary and booster vaccinations compared with no vaccination (analysis population 1) and (**B**) NVX-CoV2373 booster vaccination compared with no booster vaccination (analysis population 2). Parameters for which CIs were not available were set within ±20% of the value. The price of the NVX-CoV2373 vaccine (JPY 9000 per vaccination) was set within the range of ±50%. The vertical lines represent the ICERs for the base-case scenarios. A horizontal bar was generated for each parameter. The width of the bars indicates the potential effect of the parameters on the ICER when parameters are changed within their ranges. The red sections of each bar show high values of parameter ranges, and the blue sections show low values. [a] 95% CI was used as the range for the sensitivity analysis. [b] Given that the distribution of clinical outcomes is not calculated correctly when the analysis is performed with an upper limit of 99.7%, the analysis was performed with the upper limit set to 98.0%, a point at which a reasonable distribution of clinical outcomes is obtained. [c] The ICER was JPY 5 million or greater when the value for VE against infection was ≤61%, and it became dominant when the value was ≤49%. [d] The ICER became dominant when the value for VE against severe disease was ≤77%. CI: confidence interval; COVID-19: coronavirus disease 2019; ICER: incremental cost-effectiveness ratio; JPY: Japanese yen; QALY: quality-adjusted life-year; VE: vaccine efficacy.

Figure S2. Probabilistic Sensitivity analysis in analysis population 1.



(**A**) Scatter plot of incremental costs and QALYs. (**B**) Cost-effectiveness acceptability curve. At a threshold of JPY 5 million per QALY, NVX-CoV2373 primary and booster vaccinations had a probability of 81.5% for being cost-effective. JPY: Japanese yen; QALY: quality-adjusted life-year; WTP: willingness-to-pay.

Figure S3. Probabilistic Sensitivity analysis in analysis population 2.



(**A**) Scatter plot of incremental costs and QALYs. (**B**) Cost-effectiveness acceptability curve. At a threshold of JPY 5 million per QALY, an NVX-CoV2373 booster vaccination had a probability of 75.9% for being cost-effective. JPY: Japanese yen; QALY: quality-adjusted life-year; WTP: willingness-to-pay.

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