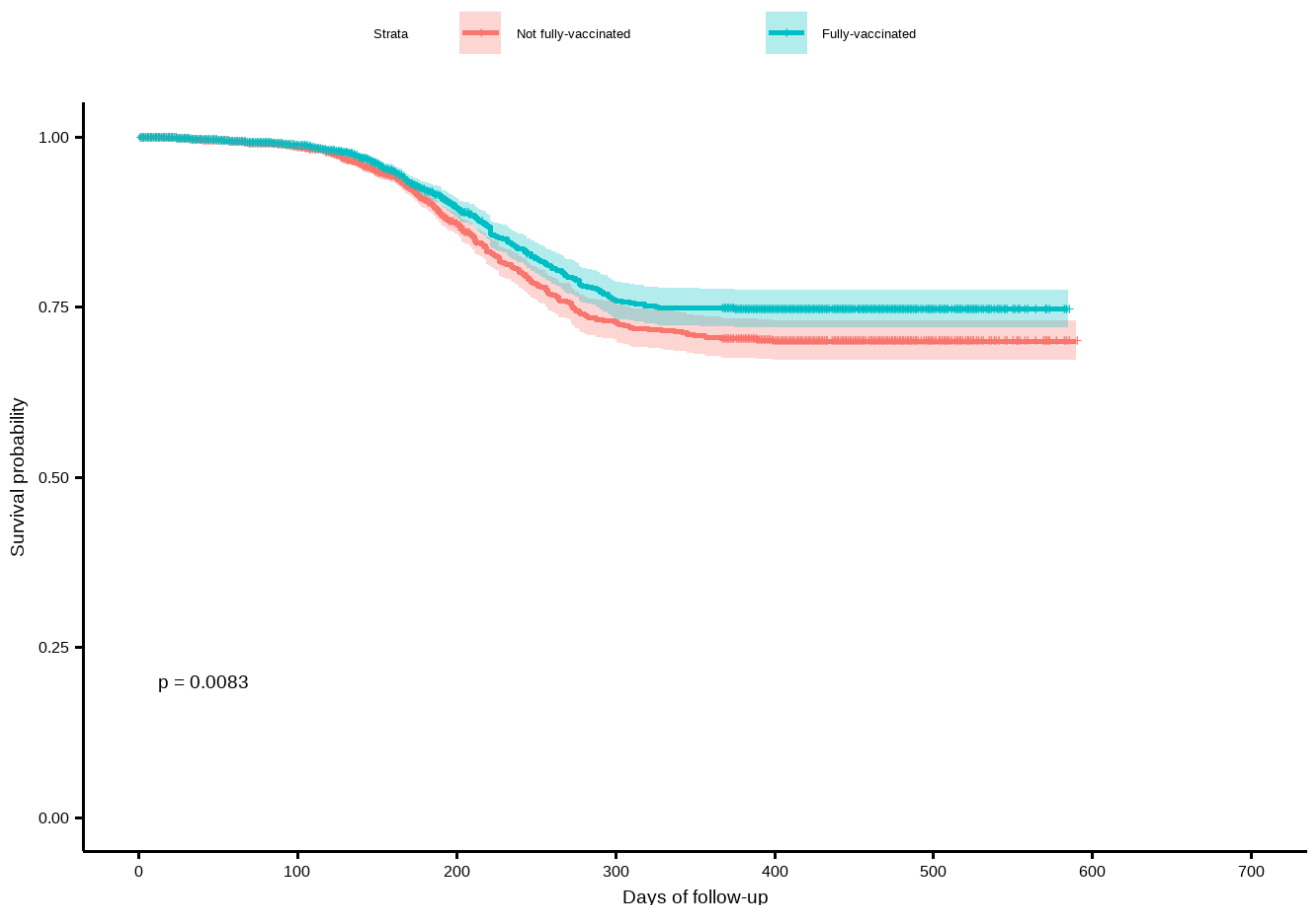


BY-COVID - WP5 - Baseline Use Case: COVID-19 vaccine effectiveness assessment

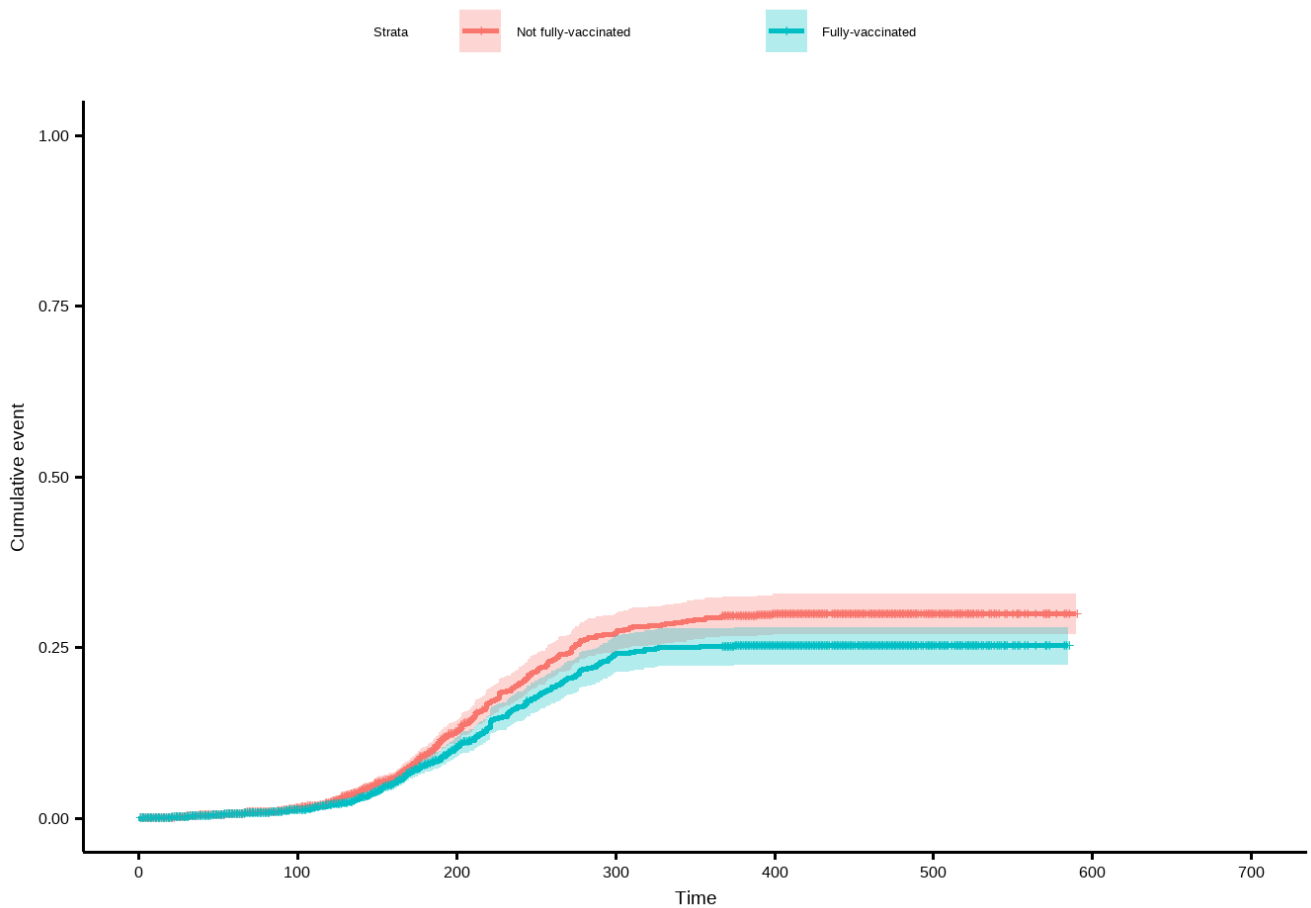
Survival analysis

Survival plot

We estimate the survival function using the Kaplan-Meier estimator and represent this function visually using a Kaplan-Meier curve, showing the probability of not getting infected by SARS-CoV-2 at a certain time after onset of follow-up. The survival function is estimated for the control and intervention group.



The cumulative incidence of the event (SARS-CoV-2 infection) was additionally plotted.



Survival (time-to-event)

The probability of not getting infected by SARS-CoV-2 beyond a certain time after onset of follow-up (survival function, estimated using the Kaplan-Meier estimator) is reported for different periods.

Strata	Time	Number at risk	Cumulative sum of number of events	Cumulative sum of number censored	Survival	Std. Error
Not fully vaccinated	0	8126	0	0	1.0000000	0.0000000
Not fully vaccinated	100	2763	66	5318	0.9847823	0.001955
Not fully vaccinated	200	847	263	7036	0.8726674	0.008076

Strata	Time	Number at risk	Cumulative sum of number of events	Cumulative sum of number censored	Survival	Std. error
Not fully vaccinated	300	560	376	7191	0.7281129	0.014157
Not fully vaccinated	400	438	397	7296	0.7002962	0.014864
Not fully vaccinated	500	94	397	7642	0.7002962	0.014864
Fully vaccinated	0	8126	1	0	0.9998769	0.000123
Fully vaccinated	100	2766	56	5323	0.9875784	0.001735
Fully vaccinated	200	865	218	7065	0.8959358	0.007370
Fully vaccinated	300	580	324	7223	0.7587970	0.013774
Fully vaccinated	400	467	333	7332	0.7469473	0.014114
Fully vaccinated	500	98	333	7707	0.7469473	0.014114

Median survival time

The median survival time is the time corresponding to a probability of not obtaining a SARS-CoV-2 infection probability of 0.5. (if NA, the probability of not obtaining a SARS-CoV-2 infection did not drop below 50%)

Characteristic	Median survival (95% CI)
fully_vaccinated_bl	
FALSE	— (—, —)
TRUE	— (—, —)

Cox regression and estimation of the average treatment effect

A Cox regression model was built to examine the relationship between the distribution of the probability of not obtaining a SARS-CoV-2 infection (survival distribution) and completing a primary vaccination schedule (covariate). The Cox proportional hazards regression model was fitted with 'fully_vaccinated_bl' as a covariate and accounts for clustering within individuals (as one individual can be re-sampled as control).

A hazard ratio (HR) is computed for the covariate 'fully_vaccinated_bl'. A hazard can be interpreted as the instantaneous rate of SARS-CoV-2 infections in individuals that are at risk for obtaining an infection (Cox proportional hazards regression assumes stable proportional hazards over time). A HR < 1 indicates reduced hazard of SARS-CoV-2 infection when having completed a primary vaccination schedule whereas a HR > 1 indicates an increased hazard of SARS-CoV-2 infection.

	Parameter estimate	SE coefficient	Robust SE	P-value	Hazard Ratio (HR) (95% CI for HR)
fully_vaccinated_blTRUE	-0.196	0.074	0.095	0.039	0.822 (0.636, 1.008)

The overall significance of the model is tested.

	Test statistic	Df	P-value
Likelihood ratio test	6.976777	1	0.008257419
Wald test	4.270000	1	0.038863280
Score (logrank) test	6.970222	1	0.008287722
Robust score test	3.980840	1	0.046020612

Proportional hazards during the study period might be unlikely. As such, the RMST and RMTL ratios are additionally calculated, providing an alternative estimate for the the Average Treatment Effect (ATE), without requiring the proportional hazards assumption to be met.

Arm	Measure	Estimate	SE	CI.lower	CI.upper
fully_vaccinated_bl==FALSE	RMST	319.029	2.153	314.809	323.250
fully_vaccinated_bl==TRUE	RMST	326.172	2.014	322.224	330.119
fully_vaccinated_bl==FALSE	RMTL	45.971	2.153	41.750	50.191
fully_vaccinated_bl==TRUE	RMTL	38.828	2.014	34.881	42.776

Measure	Estimate	CI.lower
RMST (fully_vaccinated_bl==TRUE)- (fully_vaccinated_bl==FALSE)	7.142	1.363
RMST (fully_vaccinated_bl==TRUE)/(fully_vaccinated_bl==FALSE)	1.022	1.004
RMTL (fully_vaccinated_bl==TRUE)/(fully_vaccinated_bl==FALSE)	0.845	0.737

