# Hybrid immunity and protection against infection during the Omicron wave in Malta

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## Abstract

Background: By December 2021, administration of the third dose of COVID-19 vaccinations coincided with the spread of the Omicron variant in Europe. Questions had been raised on protection against infection conferred by previous vaccination and/or infection. Method: Our study population (n = 252,433) included all those in the COVID-19 vaccination registry in Malta who were vaccinated with only 2 doses equivalent by 15th December 2021, and not vaccinated with an additional dose by 8th March 2022, and alive by 8th March 2022. Data were then matched with the national testing database (all RT-PCR/Rapid Diagnostic Tests - RDT tests) until 8th March. We collected vaccination status, vaccine brand, vaccination date, infection history, and age. Using logistic regression, we examined different combinations of vaccine dose, prior infection status and time, and the odds of infection during the Omicron period (December 15th, 2021 onwards). Results: Results found that participants infected with Sars-Cov-2 prior to the Omicron wave had a significantly lower odds of being infected with the Omicron variant. Additionally, the more recent the infection and the more recent the vaccination, the lower the odds of infection. Receiving a third dose within 20 weeks of the start of the Omicron wave in Malta offered similar odds of infection as receiving a second dose within the same period. Conclusion: Time since vaccination is a strong determinant factor against infection, as was previous infection status and the number of doses taken. This finding reinforces the importance of future booster dose provision especially to vulnerable populations.

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Forest Plot showing odds ratios for Omicron infection with different vaccination groups

Number of doses	Vaccine type	Weeks from vaccination	Infected pre-Omicron	Weeks since infection		OR (95% CI)
2	mRNA	> 20	No			<ul> <li>1.00 (reference)</li> </ul>
2	mRNA	> 20	Yes	> 20	<b>—</b>	0.66 (0.55, 0.78)
2	mRNA	> 20	Yes	< 20		0.05 (0.01, 0.14)
2	mRNA	< 20	No		Hel	0.37 (0.34, 0.39)
2	mRNA	< 20	Yes	> 20	<b>⊢</b> ∎→-1	0.20 (0.15, 0.28)
2	mRNA	< 20	Yes	< 20	H <b>B</b> I	0.03 (0.00, 0.15)
2	Adenoviral	> 20	No		H <b>a</b> -H	0.69 (0.66, 0.73)
2	Adenoviral	> 20	Yes	> 20	<b></b> 0	0.49 (0.40, 0.59)
2	Adenoviral	> 20	Yes	< 20	<b>⊢−−</b> ■	0.20 (0.11, 0.33)
2	Adenoviral	< 20	No			0.15, (0.13, 0.17)
2	Adenoviral	< 20	Yes	> 20	<b>⊢−0</b> −−−−+	0.11 (0.03, 0.25)
2	Adenoviral	< 20	Yes	< 20		0.13 (0.01, 0.59)
3	mRNA	< 20	No		Hel	0.35 (0.33, 0.37)
3	mRNA	< 20	Yes	> 20	H <b>H</b> H	0.25 (0.21, 0.30)
3	mRNA	< 20	Yes	< 20	<b>⊢</b> ∎—1	0.10 (0.04, 0.19)
3	Adenoviral	< 20	No		101	0.34 (0.32, 0.36)
3	Adenoviral	< 20	Yes	> 20	H <b>e</b> H	0.15 (0.11. 0.20)
3	Adenoviral	< 20	Yes	< 20	0.2 0.4 0.6 0.8 Odds ratio with 95% confidence interv	0.02 (0.00, 0.10

#### Forest Plot showing odds ratios for Omicron infection, comparing mRNA and Adenoviral vaccine groups

Combination of doses, time and infection	mRNA vaccines     Adenoviral vaccines
2 doses, > 20 weeks since vaccination, No previous infection	l•-I
2 doses, > 20 weeks since vaccination, Previously infected, > 20 weeks since infection	
2 doses, > 20 weeks since vaccination, Previously infected, < 20 weeks since infection	
2 doses, < 20 weeks since vaccination, No previous infection	H#1
2 doses, < 20 weeks since vaccination, Previously infected, > 20 weeks since infection	
2 doses, < 20 weeks since vaccination, Previously infected, < 20 weeks since infection	₩
3 doses, < 20 weeks since vaccination, No previous infection	
3 doses, < 20 weeks since vaccination, Previously infected, > 20 weeks since infection	⊨
3 doses, < 20 weeks since vaccination, Previously infected, < 20 weeks since infection	<b>⊨</b> ■
	0 0.2 0.4 0.8 0.8 1 1.2 Odds ratio with 95% confidence interval

0.2 0.4 0.6 0.8 1 Odds ratio with 95% confidence interval