

## Levels of SARS-CoV-2 antibodies among fully vaccinated individuals with Delta or Omicron variant breakthrough infections

### Supplementary note 1. Delta variant occurrence in Denmark.

Information regarding the development of Alpha and Delta SARS-CoV-2 variants in Denmark during the study period may be found using the following link <https://files.ssi.dk/covid19/virusvarianter/status/virusvarianter-covid19-04082021-m143> for the report "Status for udvikling af SARS-CoV-2 Varianter der overvåges i Danmark" ("Status of the development of SARS-CoV-2 variants under surveillance in Denmark") of the 4th of August 2021.

### Supplementary note 2. Omicron occurrence in Denmark.

Number of confirmed SARS-CoV-2 cases, Omicron cases, samples tested with variant PCR, percentage with variant PCR and percentage of Omicron cases during the study period may be found through the following link: <https://files.ssi.dk/covid19/omikron/statusrapport/rapport-omikronvarianten-07012022-27nk> Statens Serum Institut, "Rapport om Omikronvarianten" ("Report about the omicron variant") 7. January 2022.

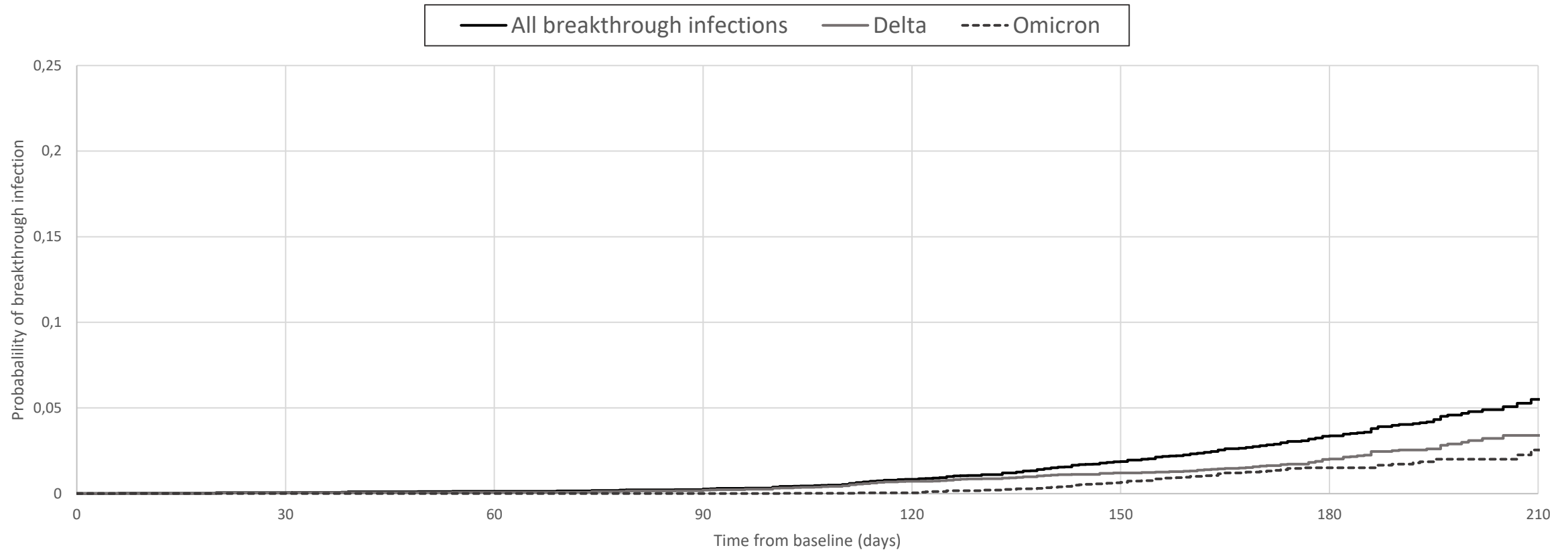
### Supplementary table 1. Variant classification of breakthrough infections

	Variant sequence confirmed		Total
	Yes, N (%)	No, N (%)	N
Alpha	3 (75.0)	1 (25.0)	4
Delta	120 (94.5)	7 (5.5)	127
Omicron	40 (11.0)	324 (89.0)	364
Unknown	0	9 (100)	9
Total	163 (32.3)	341 (67.7)	504

**Supplementary table 2. Reasons for exclusion.**

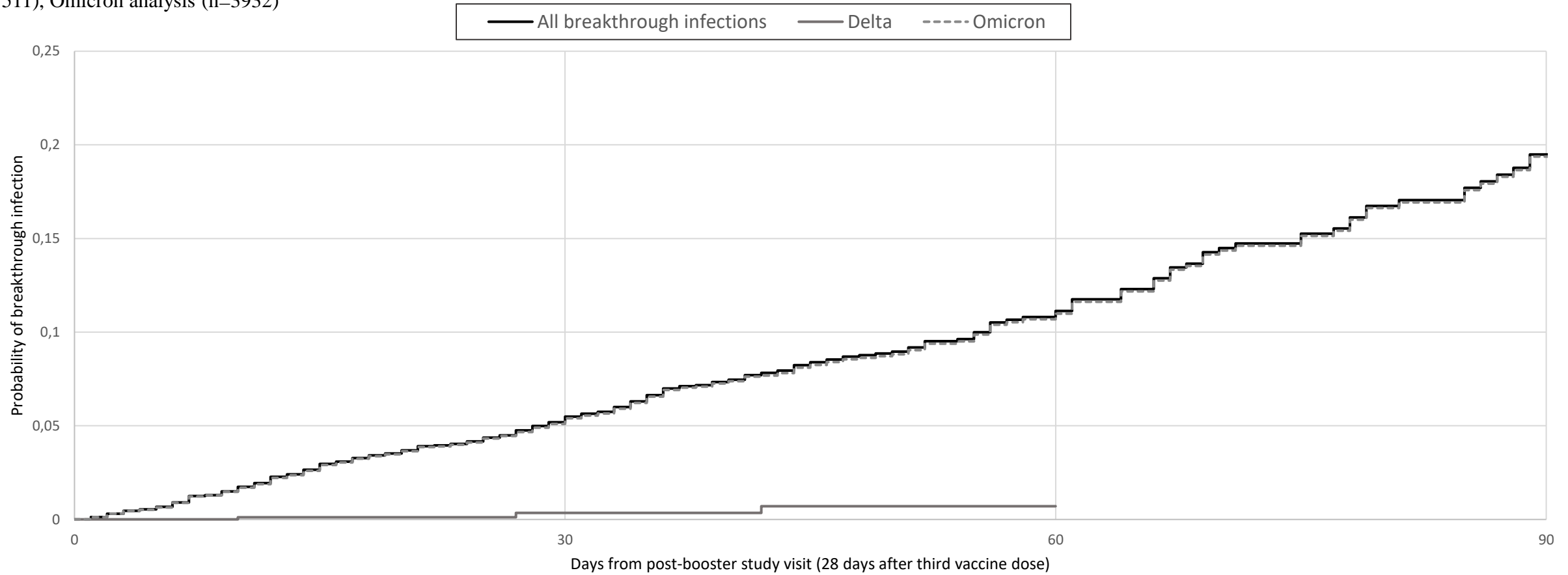
<i>Total included</i>	<i>Reason for exclusion</i>
6950	All participants
6927	Consent withdrawn and requested data deleted
6926	Aged under 18
6925	No vaccine data registered
6918	Non-standard vaccine regimen
6910	Only received 1 dose of vaccine
6525	Previously infected with SARS-CoV-2
6421	No-follow-up (withdrew before baseline)
6076	No follow-up antibody measurements

Supplementary figure 1. Time from baseline to breakthrough infection after initial vaccination by viral variant shown as Kaplan Meier plots. All infections analysis n=6076, Delta infections analysis n=6063, Omicron analysis n=5050



Time		0	30	60	90	120	150	180	210
All	Failed	0	3	8	16	50	110	171	204
	At risk	6076	6071	6053	6036	5975	5135	2882	319
Delta	Failed	0	2	4	12	43	70	100	123
	At risk	6063	6061	6049	6033	5861	5054	5811	302
Omicron	Failed	0	0	0	0	2	31	60	70
	At risk	5050	5050	5050	5046	5019	4257	2127	279

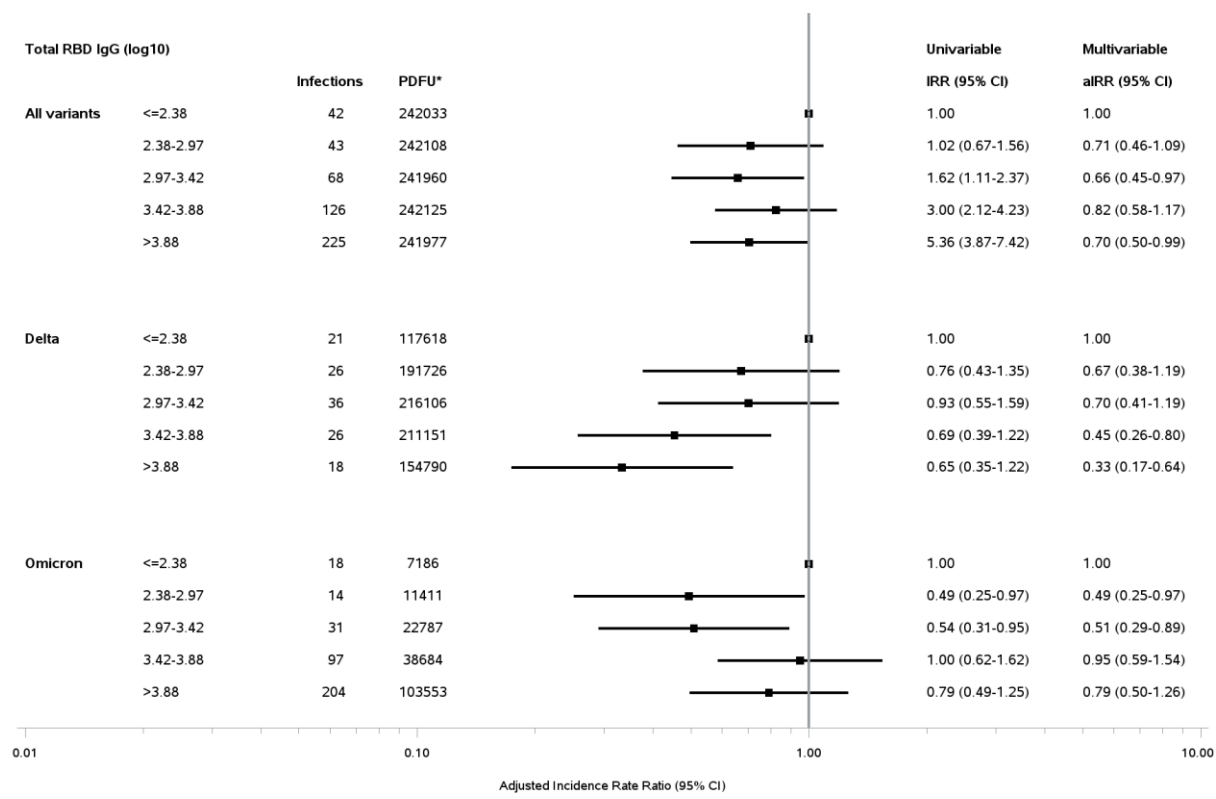
Supplementary figure 2. Time from baseline to breakthrough infections after booster vaccination shown as Kaplan Meier plots. All infections analysis (n=3939), Delta infections analysis (n=1511), Omicron analysis (n=3932)



Time		0	30	60	90
All	Failed	0	171	245	279
	At risk	3939	1853	569	214
Delta	Failed	0	2	3	-
	At risk	1511	344	129	-
Omicron	Failed	0	168	241	275
	At risk	3932	1850	568	214

**Supplementary figure 3: Incidence rate ratios (IRR) and adjusted incidence rate ratios (aIRR) for breakthrough infections.** Calculated using a Poisson regression analysis for each quintile of SARS-CoV-2 anti-receptor binding domain (RBD) IgG log<sub>10</sub> BAU, stratified by viral variant. Participants were censored at the time of third SARS-CoV-2 vaccination and re-entered the analysis at the time of post-booster visit.

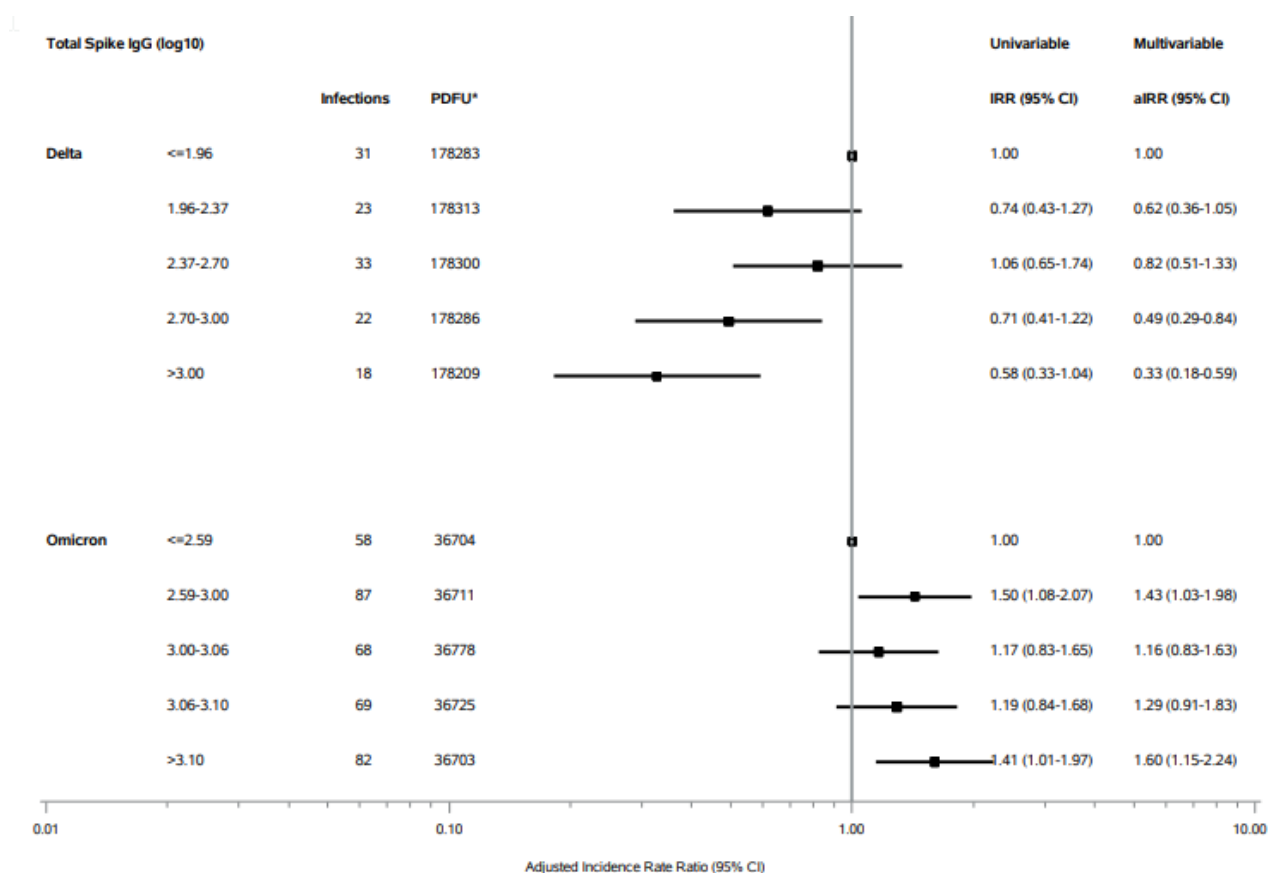
The multivariable models were adjusted for age at enrolment (per year later), gender (male vs female), healthcare worker (no vs yes) and transmission level with two-sided chi-squared tests for each variable in the model. The multivariable model for the Omicron variant did not include transmission level as all Omicron breakthrough infections occurred during the very high transmission period. All variants analysis (n=6076), Delta analysis (n=6063), Omicron (n=5050). The data presented are the aIRR and 95% confidence intervals from the multivariable models.



**Supplementary figure 4:**

Sensitivity analysis forest plot of the adjusted incidence rate ratios (aIRR) for breakthrough infections, using total anti-spike antibody levels in quintiles specific for each variant. Incidence rate ratios (IRR) and adjusted incidence rate ratios (aIRR) for breakthrough infections calculated using a Poisson regression analysis for each quintile of SARS-CoV-2 anti-spike IgG log10 BAU specific for each viral variant. Participants were censored at the time of third SARS-CoV-2 vaccination and re-entered the analysis at the time of post-booster visit. The multivariable models were adjusted for age at enrolment (per year later), gender (male vs female), healthcare worker (no vs yes) and transmission level with two-sided chi-squared tests for each variable in the model. The multivariable model for the Omicron variant did not include transmission level as all Omicron breakthrough infections occurred during the very high transmission period. Delta analysis (n=6063), Omicron (n=5050). The data presented are the aIRR and 95% confidence intervals from the multivariable models.

\*Person days of follow-up



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