

Effect of mRNA vaccination and previous infections on SARS-CoV-2 transmission across four variants: adjusted analysis of 111'432 declared contacts

Supplementary material

Methods

Link between the index case and its contact

The type of link between the index case and its contact was coded as indicated in the column “initial value” in the original form, and recoded as presented in the “recoded value”:

Live under the same roof	Same roof
Intimate contact	Intimate or familial
Familial relation	Other
Professional relation	Other
School	Other
University	Other
Leisure/hobbies	Other
Healthcare	Other
Other	Other

Symptoms

The following symptoms were recording in ARGOS. These symptoms could be filled during any follow-up call. Index case was considered to have a symptom if any of the following was filled during any follow-up. He was considered coughing if he indicated any type of cough during any follow-up call.

Dry cough
Productive cough
Dyspnoea

Fever
Chills
Tiredness or Fatigue
Muscle and/or joint pain
Headache
Runny/stuffy nose
Sore throat
Loss of taste/smell
Conjunctivitis
Abdominal pain
Nausea/vomiting
Diarrhoea
Skin eruption
Other
Digestive symptoms
Cough
ear, nose, throat symptoms

Personal vulnerability

Personal vulnerability was calculated as a binary variable. A person was considered vulnerable if any of the following applied:

- The address of the person corresponded to a highly subsidised living (habitation bon marché in Switzerland)
- The address of the person corresponded to one of the immigrant hostel in Geneva or one of the institution to accommodate person without living
- The address of the person was the one of the social administrative tribunal
- The person indicated that he/she did not want to be controlled by the police, because of its illegal situation
- The person declared to have difficulties to make the end meet

Missing data

Missing data were handled using multiple imputation with chained equations (20 samples, 5 iterations) at the person, infection or contact level:

- Missing height, weight, birth year, gender or living socio-economic index were imputed at the person level using predictive mean matching for height, weight and birth year, logistic regression imputation for gender and polytomous regression imputation for the socio-economic index
- Presence or absence of symptoms, and presence or absence of cough was imputed at the infection level using logistic imputation considering also the age, the gender, the body mass index and the SARS-COV2 variant
- Missing contact type and missing immunity/vaccinal status were imputed at the contact level using polytomous regression imputation and considering in the equation the fact of living at the same address, the fact of being contaminated by the index case, and the SARS-cov2 variant.

Population of Geneva

The following table provides for the entire population of Geneva in 2021 the number and percentage of the age categories considered in the study:

age	Total Number	Percentage
0-17	94,085	18.53
18-64	329,611	64.93
65+	83,960	16.54

Results

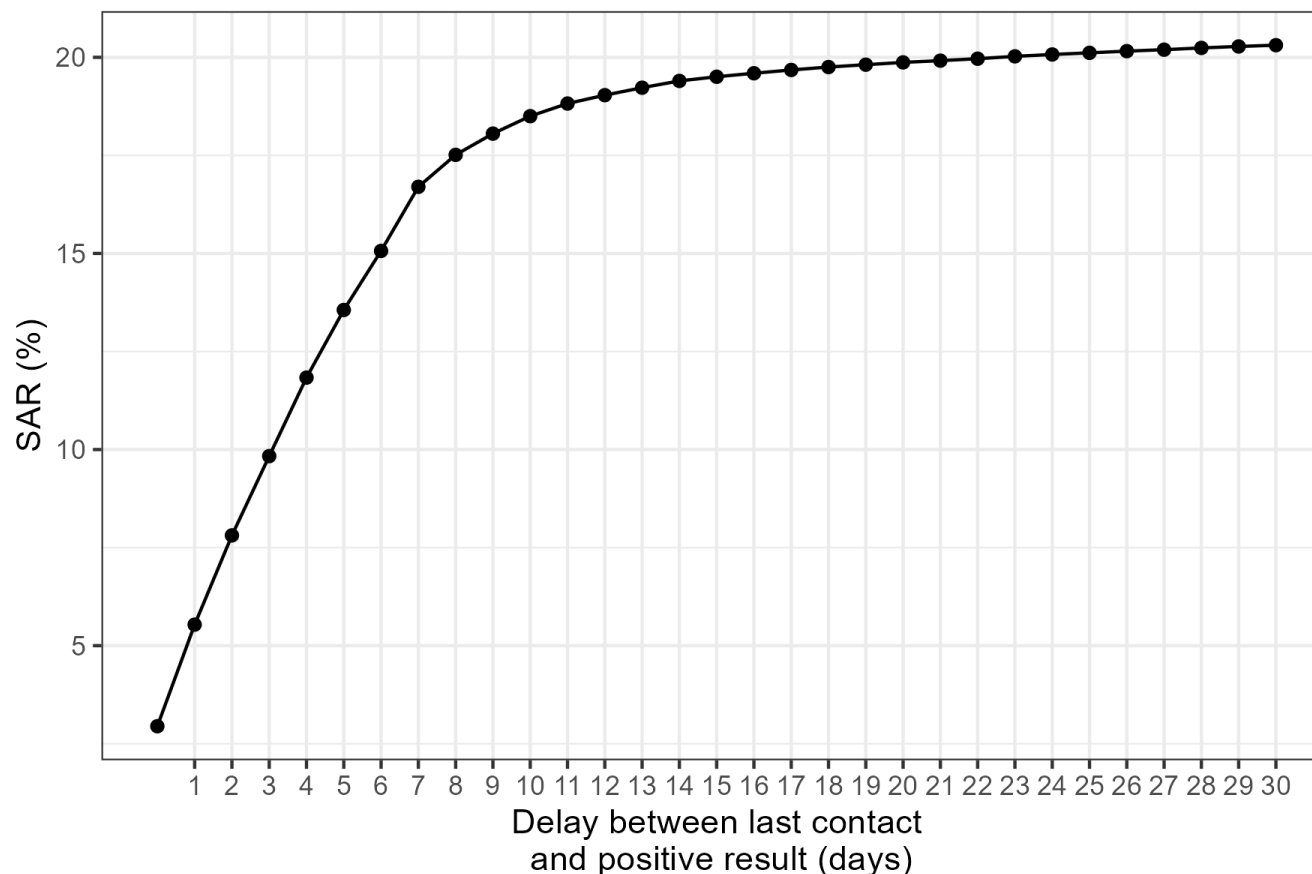


Figure S1: raw SAR as a function of the delay between test result of the index and test result of the contact.

Univariable and multivariable analysis

Some of the variables had a different effect when performing a univariable analysis or when adjusting for all co-variate (see supplementary table S2). The main differences concerned the effect of symptoms during the alpha wave (+12.3pp in the univariable model and +7.5pp in the adjusted model) and in a lesser extend during the EU1 wave (4.8 pp in the univariable model and 2pp in the adjusted model). This difference was caused by the adjustment for the cough and for demographic variables.

The Immune status of the contact had different effects between the univariable and adjusted model. The effect of being vaccinated less than 6 months ago for the contact was greater in the adjusted analysis, especially for the omicron wave, where the univariable analysis yielded a SAR increase of 2.4pp when the multivariate analysis indicated a reduction of the SAR of -2.9pp.

The SAR reduction associated with the fact of being previously infected was larger in the adjusted analysis than in the univariable analysis, especially during the EU1, delta

and omicron. These differences were mainly due to the adjustment for the propensity of the contacts to perform tests, measured by the number of COVID-19 tests performed during the last 3 months. In a sensitivity analysis including an interaction term between the immune status of the contact and the number of tests performed the last 3 months (see supplementary table S2), we observed a highly significant interaction between these two variables. This interaction effect is mainly driven by the fact that non-vaccinated and vaccinated more than 6 months ago individuals who didn't do any tests in the last 3 months had low SAR compared to those with a higher propensity to test. In contrast, previously infected individuals had very low SAR irrespective of their number of previous tests.

On the opposite, the protection of being previously infected for the index case was lowered in the adjusted analysis when compared with the univariable analysis. The adjustment for symptoms and cough explained 2pp of this difference, and the adjustment immune status of the contact explained the rest of this difference.

		EU1	alpha	delta	omicron
Index	Immunity: previously infected < 6months (NVNI)	-10.7*** [-14.5,-6.8]	-18.7*** [-22.9,-14.6]	-13.8*** [-20.7,-6.9]	-11.5*** [-17.8,-5.3]
Index	Immunity: previously infected > 6months (NVNI)	-12.7*** [-17.9,-7.4]	-10.6* [-19.3,-2.0]	-12.8*** [-15.7,-9.9]	-7.1*** [-10.4,-3.8]
Index	Immunity: vaccinated > 6 months (NVNI)		-4.7* [-9.0,-0.4]	-6.5*** [-7.7,-5.3]	-5.4*** [-7.1,-3.8]
Index	Immunity: vaccinated < 6 months (NVNI)			-1.0 [-3.1,1.1]	-0.4 [-2.2,1.4]
Index	Immunity: hybrid (NVNI)		11.6 [-29.6,52.8]	-10.6*** [-15.9,-5.3]	-8.2*** [-11.0,-5.4]
Index	women (men)	-0.6 [-1.5,0.2]	0.4 [-1.1,2.0]	-0.0 [-1.1,1.0]	-1.9** [-3.1,-0.7]
Index	age 0-17 (18-64)	-2.9*** [-4.3,-1.5]	-8.2*** [-9.9,-6.4]	-0.3 [-1.4,0.8]	1.6* [0.2,3.1]
Index	age 65+ (18-64)	4.2*** [2.4,6.0]	0.2 [-3.4,3.9]	-0.3 [-2.8,2.1]	1.5 [-2.4,5.3]
Index	Obese (not obese)	1.8* [0.2,3.3]	3.6** [1.0,6.1]	0.6 [-1.4,2.5]	-1.1 [-3.3,1.0]
Index	Symptoms (no symptoms)	4.9*** [2.8,6.9]	12.3*** [10.1,14.4]	5.4*** [3.7,7.1]	5.1*** [2.4,7.9]
index	Cough (no cough)	5.9*** [5.0,6.8]	8.1*** [6.6,9.6]	2.9*** [1.9,4.0]	1.6* [0.3,3.0]
index	Immunity: cured (not vaccinated)	-11.0*** [-14.2,-7.8]	-16.3*** [-20.4,-12.3]	-12.8*** [-15.4,-10.2]	-5.5*** [-8.4,-2.5]
index	Immunity: vaccinated > 6 months (not vaccinated)			-1.8 [-3.7,0.2]	-0.8 [-2.4,0.8]
index	Immunity: vaccinated < 6 months (not vaccinated)		-5.2* [-9.4,-1.1]	-6.6*** [-7.7,-5.4]	-5.0*** [-6.4,-3.5]
index	neighbourhood poverty: sligh (wealthy)	-0.3 [-1.7,1.0]	1.1 [-1.2,3.4]	-1.1 [-2.6,0.5]	0.2 [-1.6,2.0]
index	neighbourhood poverty: moderate (wealthy)	-1.0 [-2.2,0.3]	-0.5 [-2.7,1.8]	-0.7 [-2.2,0.8]	-0.7 [-2.5,1.1]
index	neighbourhood poverty: high (wealthy)	-0.6 [-1.7,0.5]	0.7 [-1.2,2.7]	-0.9 [-2.2,0.4]	-0.9 [-2.5,0.7]
index	vulnerable (not vulnerable)	-1.1 [-2.7,0.5]	-0.5 [-3.0,2.0]	0.5 [-1.5,2.5]	-3.3* [-5.9,-0.6]
index	living: single house (building)	0.8 [-0.4,2.0]	-1.2 [-3.3,0.9]	-0.3 [-1.7,1.0]	0.1 [-1.7,1.9]
index	living: collective structure (building)	0.5 [-2.1,3.1]	-4.7* [-9.2,-0.1]	-6.0*** [-8.9,-3.0]	-1.3 [-5.1,2.5]
Index - Contact	intimate/family (housing)	-8.7*** [-9.6,-7.8]	-12.9*** [-14.4,-11.3]	-9.0*** [-10.1,-7.9]	-6.5*** [-8.3,-4.8]

		EU1	alpha	delta	omicron
Index - Contact	pro/school/daily (housing)	-10.4*** [-11.6,-9.3]	-16.3*** [-18.6,-14.0]	-12.2*** [-13.6,-10.7]	-10.7*** [-13.5,-7.9]
Contact	Immunity: previously infected < 6months (NVNI)	1.3 [-0.6,3.1]	-21.5*** [-22.9,-20.2]	-22.7*** [-23.7,-21.7]	-21.4*** [-23.0,-19.8]
Contact	Immunity: previously infected > 6months (NVNI)	-17.0*** [-18.6,-15.4]	-20.0*** [-22.4,-17.5]	-15.5*** [-17.4,-13.5]	-1.3 [-4.5,1.8]
Contact	Immunity: vaccinated < 6 months (NVNI)		-10.5*** [-12.8,-8.2]	-10.6*** [-11.6,-9.5]	9.0*** [7.1,10.9]
Contact	Immunity: vaccinated > 6 months (NVNI)		-14.9* [-17.5,-12.3]	-1.1 [-3.5,1.4]	16.7*** [14.7,18.7]
Contact	Immunity: hybrid (NVNI)		-17.5*** [-22.9,-12.2]	-21.0*** [-22.0,-20.0]	-10.5*** [-12.3,-8.7]
Contact	women (men)	0.5 [-0.1,1.2]	-1.2 [-2.3,0.0]	-0.1 [-0.9,0.7]	0.3 [-0.7,1.4]
Contact	age: 0-17 (18-64)	-12.1*** [-12.8,-11.4]	-6.8*** [-8.1,-5.5]	2.4*** [1.5,3.4]	-9.5*** [-10.6,-8.4]
Contact	65+ (18-64)	3.5*** [1.8,5.2]	-4.0** [-6.9,-1.2]	-2.5** [-4.3,-0.7]	-7.8*** [-10.8,-4.9]
Contact	N test 30days: 0 (1)	-16.6*** [-17.7,-15.5]	-10.8*** [-12.4,-9.2]	-13.5*** [-14.8,-12.2]	-15.3*** [-17.0,-13.7]
Contact	N test 30days: 2+ (1)	1.5 [-1.1,4.1]	1.0 [-1.9,3.9]	2.4* [0.1,4.6]	-4.0** [-6.9,-1.1]

Table S1: Coefficients of the univariable generalized estimating equation [Confidence Interval], providing the additional effect on the secondary attack rate for the 4 periods of dominance of the variants EU1, alpha, delta, and omicron. The reference category for each categorical variable is indicated in bold in parenthesis. The left column indicates if the variable concern the index case, the contact, or their relation.

Adjusted analysis with all immune category for index cases

		EU1	alpha	delta	omicron
	Reference	33.3*** [30.9,35.7]	31.0*** [27.8,34.1]	34.5*** [32.0,37.0]	41.0*** [37.4,44.6]
Index	Immunity: previously infected < 6months (NVNI)	-10.6*** [-14.7,-6.5]	-10.2*** [-15.3,-5.1]	-5.8 [-12.8,1.3]	-4.0 [-10.4,2.5]
Index	Immunity: previously infected > 6months (NVNI)	-7.8** [-13.3,-2.3]	-5.0 [-14.0,3.9]	-11.6*** [-14.8,-8.4]	-4.4** [-7.7,-1.1]
Index	Immunity: vaccinated < 6 months (NVNI)		-5.7* [-10.2,-1.2]	-5.5*** [-6.8,-4.2]	-6.4*** [-8.1,-4.7]
Index	Immunity: vaccinated > 6 months (NVNI)			-1.3 [-3.5,1.0]	-2.6** [-4.5,-0.7]

		EU1	alpha	delta	omicron
Index	Immunity: hybrid (NVNI)		19.3 [-13.3,51.9]	-8.5** [-13.7,-3.4]	-6.6*** [-9.5,-3.6]
Index	women (men)	-0.3 [-1.2,0.5]	0.1 [-1.4,1.5]	0.1 [-1.0,1.1]	-1.7* [-3.0,-0.4]
Index	age 0-17 (18-64)	-0.7 [-2.1,0.6]	-4.9*** [-6.6,-3.1]	-2.6*** [-3.8,-1.3]	-2.1* [-3.9,-0.4]
Index	age 65+ (18-64)	1.2 [-0.6,3.0]	3.8* [0.1,7.4]	1.5 [-0.9,4.0]	2.0 [-2.0,6.1]
Index	Obese (not obese)	1.1 [-0.4,2.5]	2.1 [-0.3,4.5]	0.5 [-1.5,2.4]	-0.8 [-3.0,1.4]
Index	Symptoms (no symptoms)	2.0 [-0.1,4.0]	7.6*** [5.1,10.0]	5.2*** [3.4,7.0]	4.5** [1.5,7.6]
index	Cough (no cough)	5.3*** [4.4,6.2]	5.5*** [3.9,7.1]	2.2*** [1.0,3.3]	1.8* [0.4,3.3]
index	neighbourhood poverty: sligh (wealthy)	-0.3 [-1.6,1.0]	0.8 [-1.4,3.0]	-1.1 [-2.6,0.5]	0.2 [-1.7,2.2]
index	neighbourhood poverty: moderate (wealthy)	-0.9 [-2.1,0.4]	-0.9 [-3.1,1.4]	-0.7 [-2.3,0.8]	-0.4 [-2.4,1.5]
index	neighbourhood poverty: high (wealthy)	-0.4 [-1.5,0.7]	0.0 [-1.9,2.0]	-1.3 [-2.7,0.1]	-0.5 [-2.3,1.2]
index	vulnerable (not vulnerable)	-0.7 [-2.3,0.8]	-1.2 [-3.6,1.3]	0.6 [-1.5,2.6]	-2.1 [-4.9,0.8]
index	living: single house (building)	0.0 [-1.2,1.3]	-1.3 [-3.4,0.8]	0.0 [-1.4,1.5]	-0.9 [-2.9,1.0]
index	living: collective structure (building)	0.7 [-1.8,3.2]	-1.9 [-6.3,2.6]	-5.1** [-8.3,-1.8]	-0.1 [-4.3,4.1]
Index - Contact	intimate/family (housing)	-9.4*** [-10.3,-8.4]	-13.1*** [-14.7,-11.6]	-8.4*** [-9.6,-7.3]	-8.0*** [-9.6,-6.3]
Index - Contact	pro/school/daily (housing)	-10.7*** [-11.9,-9.5]	-15.3*** [-17.7,-13.0]	-10.8*** [-12.5,-9.2]	-11.5*** [-13.9,-9.0]
Contact	Immunity: previously infected < 6months (NVNI)	-13.3*** [-15.4,-11.3]	-26.5*** [-28.1,-24.8]	-30.7*** [-32.1,-29.4]	-32.0*** [-33.9,-30.0]
Contact	Immunity: previously infected > 6months (NVNI)	-17.3*** [-19.3,-15.4]	-20.6*** [-23.3,-18.0]	-14.9*** [-16.8,-12.9]	-4.4** [-7.6,-1.2]
Contact	Immunity: vaccinated < 6 months (NVNI)		-13.5*** [-16.0,-11.0]	-9.5*** [-10.5,-8.4]	7.0*** [5.0,8.9]
Contact	Immunity: vaccinated > 6 months (NVNI)			0.8 [-1.6,3.3]	13.3*** [11.2,15.4]
Contact	Immunity: hybrid (NVNI)		-20.1*** [-25.8,-14.3]	-21.7*** [-22.9,-20.6]	-18.2*** [-20.4,-16.1]
Contact	women (men)	0.2 [-0.4,0.8]	-1.0 [-2.1,0.1]	-0.2 [-1.0,0.6]	-0.4 [-1.5,0.7]
Contact	age: 0-17 (18-64)	-11.7*** [-12.5,-11.0]	-8.2*** [-9.5,-6.8]	-0.2 [-1.3,0.8]	-4.8*** [-6.2,-3.4]
Contact	65+ (18-64)	4.1*** [2.4,5.8]	1.2 [-1.7,4.1]	-1.4 [-3.2,0.3]	-6.5*** [-9.6,-3.4]
Contact	N test 30days: 0 (1)	-16.3*** [-17.4,-15.1]	-11.1*** [-12.7,-9.5]	-13.3*** [-14.6,-12.0]	-17.0*** [-18.6,-15.5]
Contact	N test 30days: 2+ (1)	1.3 [-1.2,3.9]	1.7 [-1.0,4.4]	3.0** [1.1,4.8]	-0.1 [-2.0,1.8]

Table S2: Coefficients of the multivariate generalized estimating equation [Confidence Interval], providing the additional effect on the reference secondary attack rate (first line), for the 4 periods of dominance of the variants EU1, alpha, delta, and omicron. The reference category for each categorical variable is indicated in bold in parenthesis. The left column indicates is the variable concern the index case, the contact, or their relation. p values are indicated with *. *: 0.01<p<0.05, **:0.001<p<0.01, ***: p<0.001

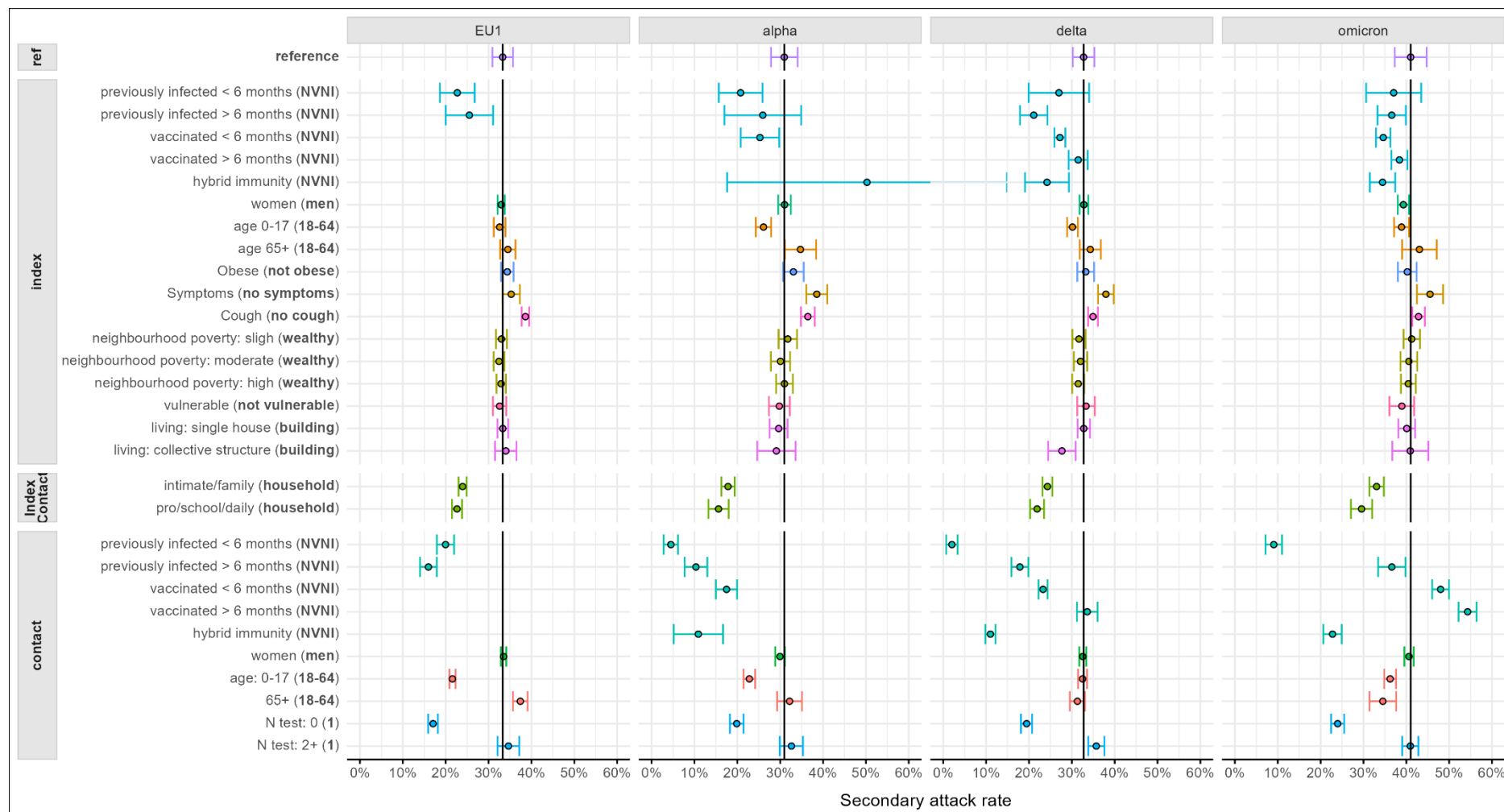


Figure S2: Adjusted Secondary Attack Rate (SAR) stratified per variant (EU1, alpha, delta and omicron), with the reference value indicated with a vertical line (reference of each covariate is indicated in bold in parenthesis). This multivariate analysis considers the effect of the index case gender, age, obesity, presence of symptoms, presence of cough, immunity status, neighbourhood socio-economic condition, vulnerability and type of living; the link between the index case and its contacts, and for the contact persons, their gender, age, number of tests performed the three months before the contact date with the index case, and their immunity status. The reference index case - contact relation of this multivariate analysis is the contact between two men of age below 65 living at the same place, the index being not vaccinated not infected (NVNI), not obese, living in a wealthy neighbourhood and being not a vulnerable person, living in a housing building, and the contact person being a NVNI adult men who performed one COVID19 test during the last 3 month preceding the contact.

Adjusted analysis stratified per gender

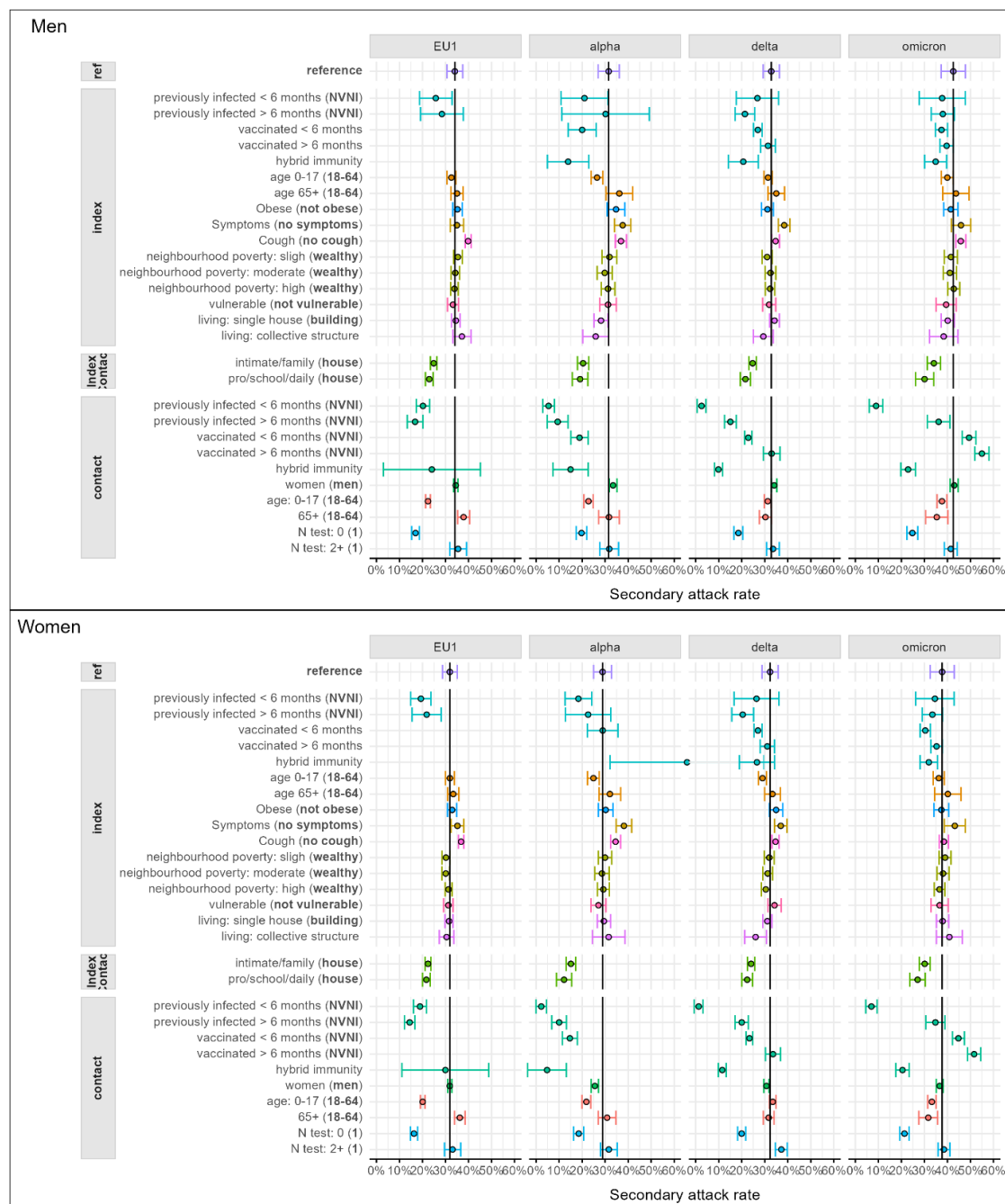


Figure S3: Adjusted Secondary Attack Rate (SAR) stratified per variant (EU1, alpha, delta and omicron) and gender, with the reference value indicated with a vertical line

(reference of each covariate is indicated in bold in parenthesis). This multivariate analysis considers the effect of the index case gender, age, obesity, presence of symptoms, presence of cough, immunity status, neighbourhood socio-economic condition, vulnerability and type of living; the link between the index case and its contacts, and for the contact persons, their gender, age, number of tests performed the three months before the contact date with the index case, and their immunity status. The reference index case - contact relation of this multivariate analysis is the contact between two men of age below 65 living at the same place, the index being not vaccinated not infected (NVNI), not obese, living in a wealthy neighbourhood and being not a vulnerable person, living in a housing building, and the contact person being a NVNI adult men who performed one COVID19 test during the last 3 month preceding the contact.

Adjusted analysis with interaction term between contact immunity and propensity of contact to perform tests

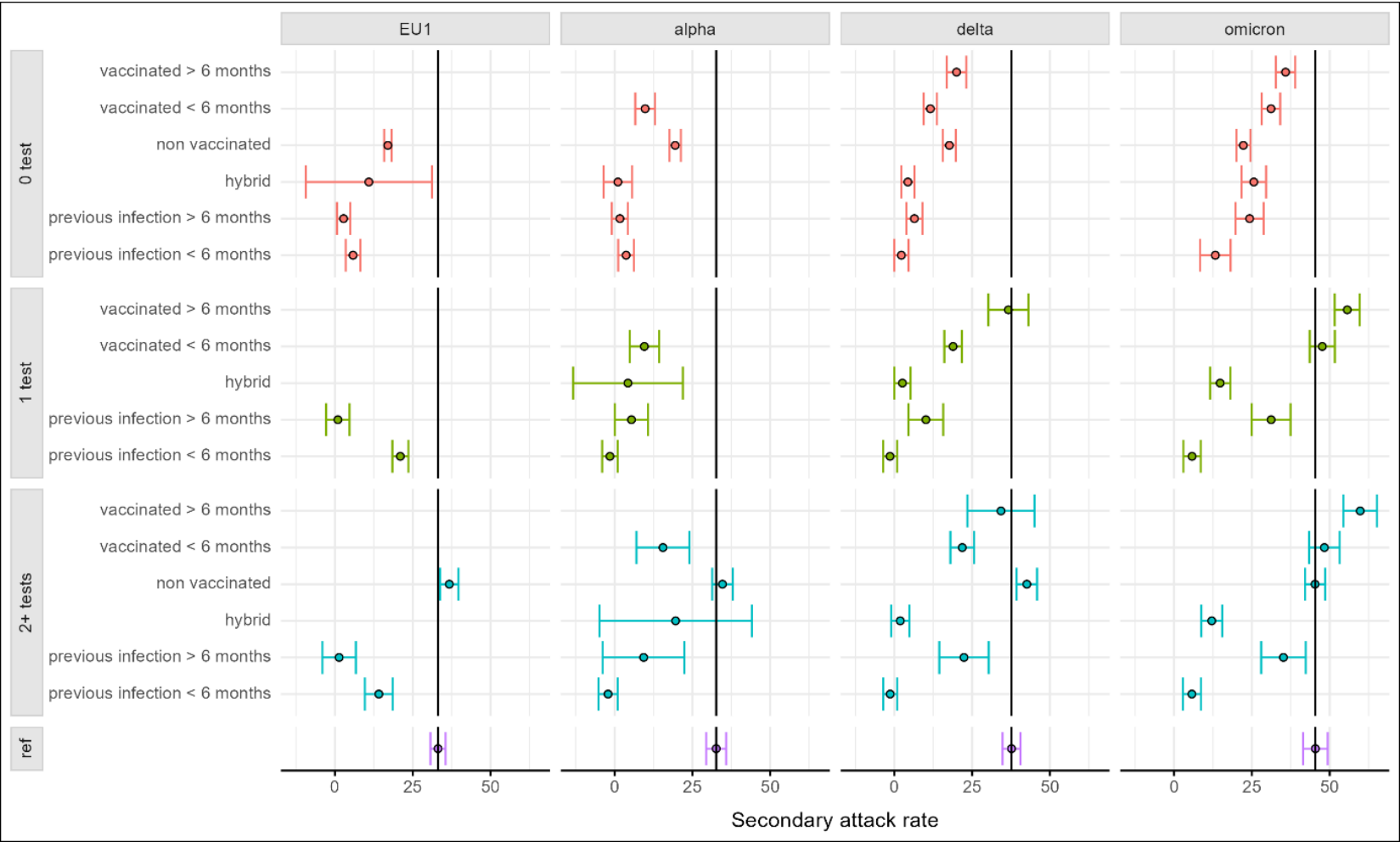


Figure S4: Adjusted secondary attack rate, displayed per immune status of the contact and number of tests performed by the contact during the 90 days preceding its last encounter with the index case

Immune status contact	Number of tests 3 months prior to contact	EU1	alpha	delta	omicron
cured<6	0 test	-27.3*** [-29.7,-24.9]	-28.9*** [-31.5,-26.4]	-35.4*** [-37.7,-33.1]	-32.2*** [-37.1,-27.2]
cured>6	0 test	-30.3*** [-32.5,-28.2]	-30.9*** [-33.5,-28.3]	-31.2*** [-33.8,-28.6]	-21.1*** [-25.6,-16.6]
hybrid	0 test	-22.2 [-42.5,-1.9]	-31.6*** [-36.1,-27.0]	-33.3*** [-35.4,-31.2]	-19.8*** [-23.8,-15.8]
NVNI	0 test	-16.1*** [-17.3,-14.9]	-13.2*** [-15.0,-11.4]	-20.0*** [-22.0,-17.9]	-23.2*** [-25.4,-20.9]
Vaccinated ac<6	0 test		-22.8*** [-26.0,-19.7]	-26.1*** [-28.2,-23.9]	-14.3*** [-17.3,-11.3]
Vaccinated >6	0 test			-17.7*** [-20.8,-14.5]	-9.6*** [-12.7,-6.5]
cured<6	1 test	-12.1*** [-14.7,-9.5]	-34.1*** [-36.6,-31.7]	-39.0*** [-41.3,-36.8]	-39.6*** [-42.4,-36.9]
cured>6	1 test	-32.2*** [-35.9,-28.4]	-27.2*** [-32.5,-21.9]	-27.5*** [-33.1,-21.9]	-14.2*** [-20.5,-8.0]
hybrid	1 test		-28.4** [-46.0,-10.7]	-35.1*** [-37.7,-32.4]	-30.6*** [-33.9,-27.4]
Vaccinated <6	1 test		-23.1*** [-27.8,-18.4]	-18.8*** [-21.6,-16.0]	2.2 [-1.8,6.3]
Vaccinated >6	1 test			-1.0 [-7.4,5.4]	10.2*** [6.2,14.3]
cured<6	2+ tests	-19.0*** [-23.5,-14.5]	-34.7*** [-37.8,-31.6]	-39.0*** [-41.2,-36.8]	-39.7*** [-42.6,-36.8]
cured>6	2+ tests	-31.8*** [-37.1,-26.4]	-23.3*** [-36.4,-10.2]	-15.3*** [-23.2,-7.3]	-10.3** [-17.4,-3.1]
hybrid	2+ tests		-13.0 [-37.5,11.5]	-35.8*** [-38.7,-32.8]	-33.3*** [-36.7,-30.0]
NVNI	2+ tests	3.6* [0.7,6.6]	2.0 [-1.3,5.3]	4.9** [1.6,8.2]	-0.1 [-3.4,3.1]
Vaccinated <6	2+ tests		-17.1*** [-25.6,-8.6]	-15.8*** [-19.7,-12.0]	2.9 [-2.0,7.8]
Vaccinated >6	2+ tests			-3.4 [-14.2,7.4]	14.4*** [9.0,19.8]
	ref	33.1*** [30.7,35.5]	32.6*** [29.4,35.8]	37.6*** [34.8,40.5]	45.4*** [41.4,49.4]

Table S3: Coefficients [Confidence Interval] of the interaction terms between the immune status of the contact and the number of tests performed by the contacts 3 months prior to the date of the interaction between contact and index, for the adjusted generalized estimating equation. These coefficients provides the additional effect on the reference secondary attack rate (last line, grey shaded), for the 4 periods of dominance of the variants EU1, alpha, delta, and omicron. The left column indicates if the variable concern the index case, the contact, or their relation. p values are indicated with *. *: 0.01<p<0.05, **:0.001<p<0.01, ***: p<0.001. NVNI : non vaccinated never infected.

