

1 **Increased risk of infection with SARS-CoV-2 Beta, Gamma, and Delta variant** 2 **compared to Alpha variant in vaccinated individuals**

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39 **Abstract**

40 The extent to which severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variants of
41 concern (VOC) break through infection- or vaccine-induced immunity is not well understood. Here,
42 we analyze 28,578 sequenced SARS-CoV-2 samples from individuals with known immune status
43 obtained through national community testing in the Netherlands from March to August 2021. We
44 find evidence for an increased risk of infection by the Beta (B.1.351), Gamma (P.1), or Delta
45 (B.1.617.2) variants compared to the Alpha (B.1.1.7) variant after vaccination. No clear differences
46 were found between vaccines. However, the effect was larger in the first 14-59 days after complete
47 vaccination compared to 60 days and longer. In contrast to vaccine-induced immunity, no increased
48 risk for reinfection with Beta, Gamma or Delta variants relative to Alpha variant was found in
49 individuals with infection-induced immunity.

50

51 **Introduction**

52 Since the worldwide spread of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) the
53 virus has been slowly but steadily evolving. Although many nucleotide mutations are synonymous,
54 multiple amino acid substitutions in functional domains of the spike protein are observed, some of
55 which with likely impact on transmissibility, disease severity and pre-existing immunity¹.

56

57 SARS-CoV-2 constellations of mutations under strong suspicion of a negative impact on virus
58 epidemiology, virulence or effectiveness of social and public health measures (including diagnostics,
59 vaccines, therapeutics) are designated Variant-of-Concern (VOC)². As of 1 September 2021, four
60 VOCs have been defined by the ECDC and WHO: Alpha (B.1.1.7, first detected in September 2020 in
61 the United Kingdom), Beta (B.1.351, first detected in May 2020 in South Africa), Gamma (P.1, first
62 detected in November 2020 in Brazil) and Delta (B.1.617.2, first detected in October 2020 in India)².

63 All four VOCs contain amino acid substitutions in the receptor binding domain (RBD) and N-terminal
64 domain (NTD) of the Spike protein, which are known to be the main target of neutralizing antibodies.
65 Several studies have shown decreased sensitivity of VOCs for convalescent and post-vaccination sera
66 *in vitro*, with little to no reduction in sensitivity for the Alpha variant, the highest reduction in
67 sensitivity for Beta and to a lesser extent for Gamma and Delta³⁻⁶.

68

69 These observations and the rapid global spread of first Alpha and later Delta sparked fear for SARS-
70 CoV-2 escape from pre-existing immunity and selection of these variants in vaccinated and
71 previously infected individuals. There are indications that the vaccine effectiveness (VE), especially
72 against SARS-CoV-2 infection or mild COVID-19, is lower for the Beta, Gamma and Delta variant⁷.
73 Less is known about the association between the observed VOCs and reinfection. Although an
74 ecological study from the UK did not find an increase in the reinfection rate for the Alpha variant
75 relative to pre-existing variants in the last quarter of 2020⁸, it needs to be determined if increased
76 risk exists of reinfection by the Beta, Gamma, or Delta variants compared to the Alpha variant.

77

78 In January 2021, the COVID-19 vaccination program was rolled out in the Netherlands, first
79 prioritizing health care workers, nursing home residents and the elderly. Current approved vaccines
80 are either based on mRNA (Comirnaty, Spikevax) or on an Adeno-based vector system (Janssen
81 COVID-19 vaccine, Vaxzevria) and are aimed to elicit a spike protein targeted humoral immune
82 response that prevents virus entry and replication^{9,10}. As of July 2021, all persons of 12 years and
83 older have been offered COVID-19 vaccination. As of November 2021, 84% of all adults were fully
84 vaccinated and 88% received at least one dose¹¹. In the vaccination program in the Netherlands,
85 Comirnaty (BNT162b2, BioNTech/Pfizer) has been used most often and has been offered to all age
86 groups (76.0% of all administered doses). Spikevax (mRNA-1273, Moderna) has been mostly used in
87 long term care facilities, health care workers, high medical risk groups and later also in the general

88 population below 60 years (8.5% of all administered doses). Vaxzevria (ChAdOx1, AstraZeneca) has
89 been used most in health care workers and the 60-65 years age group (12.1% of all administered
90 doses). Janssen COVID-19 vaccine (Ad26.COVS, Janssen) has been used most in the 50-59 years age
91 group and young adults (3.4% of all administered doses)¹². Vaccination has proven to be highly
92 effective against COVID-19, especially against hospitalization and death and reduces the secondary
93 attack rate within households^{7,13-17}.

94

95 Next to vaccination, infection with SARS-CoV-2 elicits a protective immune response though
96 reinfections do occur. Studies comparing infection rates in the first and second surge of the SARS-
97 CoV-2 pandemic between people who tested RT-PCR or antigen negative and positive in Denmark,
98 Austria and Italy reported protection against repeat infection of 81%, 91% and 94%, respectively¹⁸⁻²⁰.
99 A prospective cohort study among health care workers in the UK found a 84% lower risk of infection
100 after a previous infection²¹.

101

102 In the Netherlands, randomly selected SARS-CoV-2 RT-PCR positive specimens are sequenced to
103 continuously monitor changes in the virus²². The Alpha variant started to increase rapidly from
104 January 2021, and quickly became the dominant strain in the Netherlands. From June 2021, the
105 Delta variant increased rapidly and caused nearly all infections from August 2021 onwards. In this
106 study we aimed to investigate whether vaccine- or infection-induced immunity protects less well
107 against infection by specific variants. Therefore, we compared the variant distribution of SARS-CoV-2
108 positive individuals who were either unvaccinated, vaccinated or had a previous infection using
109 national epidemiological and molecular surveillance data from March up to August 2021.

110

111 **Methods**

112 *Data*

113 Persons testing positive for SARS-CoV-2 either by community testing or in a hospital are notified by
114 Public Health Services (PHS) to the national surveillance database. Community testing is available
115 through the PHS. Testing is encouraged in case of experiencing COVID-19-like symptoms, contact
116 with a positive case, returning from another country, or upon a positive self-test. Data relevant for
117 source and contact tracing and for surveillance is collected in the national surveillance database
118 through a telephone interview, including data on vaccination status (i.e. number of doses, type of
119 vaccine, and date of vaccination).

120

121 The Dutch national SARS-CoV-2 molecular surveillance program sequences whole virus genomes of
122 randomly selected SARS-CoV-2 positive specimens from both community testing (via PHS) and
123 hospitals, using a proper nationwide geographical distribution. In the current analysis, only samples
124 with information on vaccination status and information on previous infection can be used. This
125 information is collected in the national surveillance database and linked to sequence data using a
126 sample identifier supplied during community testing. Sequences from hospital samples (5,893 out of
127 the total 42,662 (13.8%) sequences of the SARS-CoV-2 genomic surveillance samples) and 7,464 of
128 the 36,769 sequenced community samples were excluded as these could not be linked to the
129 national surveillance database for required meta-data. In addition to randomly selected specimens,
130 additional community testing specimens were requested for partially or fully vaccinated individuals
131 as well as for cases with known prior laboratory-confirmed infection. This was done on a 3-weekly
132 basis. This additional sampling resulted in an additional 1,516 cases to be included in the study and
133 allowed for a detailed investigation of infecting variants after vaccination or reinfection. In the
134 current analyses, cases with a sampling date between March 1 and August 31, 2021, were included.

135

136 *RT-PCR amplification and Nanopore sequencing*

137 The majority of isolates were sequenced according to the following representative sequence method
138 (minimal 85.3%), additional detailed protocols are available upon request. Total nucleic acid from
139 combined nasopharyngeal and oropharyngeal swab was extracted using MagNAPure 96 (MP96) with
140 total nucleic acid kit small volume (Roche). Total nucleic acid was eluted in 50 μ l Tris EDTA buffer.
141 SARS-CoV-2 specific RT-PCR amplification and sequencing was performed using the Nanopore
142 protocol based on the ARTIC v3 amplicon sequencing protocol²³. Several modifications to the
143 protocol were made for optimization: 1) The total volume of the cDNA reaction is 12 μ l with a
144 volume of 0.4 μ l Superscript IV instead of 0.6 μ l. 2) primer concentrations and primer sequence were
145 adjusted for several amplicons to optimized amplicon yield and to match novel variants. Updated
146 primer sequences are available upon request. 3) No distinction was made on the basis of Cp value,
147 PCR was performed using 47 cycles. After the combination of PCR reactions A and B, the samples
148 were quantified with the Qubit, samples with a concentration >35ng/ μ l were diluted to 6ng/ μ l in
149 water. 5 μ l of diluted PCR mix was used in the end-prep reaction. This end-prep is incubated for 15
150 min at 20°C and 15 min at 65°C. Barcoding was performed using the NEBNext Ultra II Ligation
151 Module (E7595). In short, 1.3 μ l end-prepped DNA was added to 2.5 μ l water, 6 μ l NEBNext Ultra II
152 Ligation Master Mix, 0.2 μ l NEBNext Ligation Enhancer and 2 μ l Native barcode SQK-LSK109 (EXP-
153 NBD196). The Barcoding was incubated for 30 min at 20°C and 20 min at 65°C. Barcoded fragments
154 were washed with twice with 870 μ l short fragment buffer (SFB), once with 150 μ l ethanol and
155 eluted in 74 μ l after 4 minute incubation with the beads. Adapter ligation was performed using
156 NEBNext Quick Ligation Module (NEB) in a total volume 50 μ l using 25 μ l of AMPure XP beads. After
157 washing with 125 μ l short fragment buffer (SFB), the pellet was resuspended in 15.5 μ l elution
158 buffer. Finally, 45ng of library preparation was loaded on a flowcell (Nanopore) and sequencing was
159 performed on a R9.4.1 flow cell multiplexing 48 up to 96 samples per sequence run for a run-time of
160 30 hours on a GridION (Nanopore).

161 GridION data was analyzed to get consensus genomes, with the SARS2seq pipeline and additional
162 manual curation²⁴. These genomes were analyzed with Pangolin (version 3.1.11) and NextClade
163 (version 1.3.0) to get a final variant call^{25,26}.

164

165 *Vaccination and previous infection status*

166 Vaccination status is determined relative to the date used for statistics (DUFFS). For symptomatic
167 cases, this is the date of symptom onset or, if missing, the date of a positive test result minus 2 days.
168 For asymptomatic cases, the DUFFS is the date of positive test result. Fully vaccinated is defined as
169 having received two doses of Comirnaty, Spikevax or Vaxzevria at least 14 days before DUFFS or one
170 dose of Janssen COVID-19 vaccine at least 28 days before DUFFS. Partly vaccinated is defined as
171 having received one dose of Comirnaty, Spikevax or Vaxzevria at least 14 days before DUFFS, or two
172 doses of Comirnaty, Spikevax or Vaxzevria less than 14 days before DUFFS. A case is defined as
173 recently vaccinated after one dose of Comirnaty, Spikevax or Vaxzevria 0-13 days or Janssen COVID-
174 19 vaccine 0-27 days before DUFFS. Individuals with a subsequent positive RT-PCR or antigen test
175 result with an interval of at least 8 weeks after a previous positive test, including a period without
176 symptoms, were defined as reinfections. This is either reported in the notification by the PHS or
177 identified using record linkage by date of birth, sex, and 6-digit postal code.

178

179 *Statistical analyses*

180 We compared the proportion of the four VOCs (Alpha, Beta, Gamma and Delta variant) between
181 four immune status groups: 1) unvaccinated cases without a known previous infection (naïve), 2)
182 partly vaccinated cases without a known previous infection, 3) fully vaccinated cases without a
183 known previous infection, 4) unvaccinated cases with a previous infection. In a secondary analysis,
184 fully vaccinated cases were further stratified by time between infection and last vaccination (<60

185 days versus ≥ 60 days). Cases who were recently vaccinated, irrespective of their previous infection
186 status, were excluded from the analyses, due to a possible incomplete immune response. Since the
187 number of vaccinated cases with a previous infection was small ($n = 111$) this group was excluded.

188

189 The association between immune status and the Beta, Gamma and Delta variant was assessed using
190 logistic regression. Immune status (group 2: partly vaccinated, group 3: fully vaccinated and group 4:
191 previous infection versus group 1: naïve) was included in the model as the independent variable and
192 Beta, Gamma or Delta vs Alpha as the dependent variable. We estimated odds ratios (ORs) with 95%
193 confidence interval (CI) for any vaccine type and separately for Comirnaty, Spikevax, Vaxzevria and
194 Janssen COVID-19 vaccine. An additional analysis was performed on the time since vaccination,
195 stratifying the fully vaccinated by 14-59 and more than 60 days between complete vaccination and
196 DUFs. As calendar time is both related to vaccination uptake and prevalence of a certain variant, i.e.
197 a confounder, we included a natural cubic spline (5 knots) for calendar week of sample date in all
198 regression models. In addition, all analyses were also adjusted for 10-year age group (40-49 years as
199 reference) and sex.

200

201 **Results**

202 From 1 March to 31 August 2021, a total of 661,658 SARS-CoV-2 positive cases were notified to the
203 national surveillance database (Table 1). Of these, 38,261 (5.8%) cases were partly vaccinated,
204 25,933 (3.9%) were fully vaccinated and 10,565 (1.6%) had a known previous infection
205 (Supplementary Figure 1). Of (partly) vaccinated cases, most received Comirnaty (65.0%), followed
206 by Vaxzevria (19.3%), Janssen COVID-19 vaccine (9.8%) and Spikevax (5.9%). We included data of
207 29,305 samples that were sequenced through the national SARS-CoV-2 surveillance program (Table
208 1). In addition, 1,516 additional samples were sequenced to increase insight in variants present in
209 infections after vaccination and reinfections were included.

210

211 Up to June 2021, 94.4% (14,068 of 14,903) of infections were caused by the Alpha variant, with a
212 small proportion caused by the Beta (1.3%) and Gamma (1.3%) variant. The proportion of Delta
213 increased from 0.9% (42 of 4874) in May to 98.7% (4561 of 4620) in August 2021. This pattern was
214 observed over different immune statuses (Figure 1). In total, 17,890 (58.0%) Alpha, 209 (0.7%) Beta,
215 250 (0.8%) Gamma, 11,937 (38.7%) Delta and 535 (1.7%) other variant sequences were observed.

216

217 Logistic regression analysis showed that full vaccination was significantly associated with infection
218 with the Beta, Gamma or Delta variant compared to the Alpha variant (adjusted OR: 3.1 (95% CI: 1.3-
219 7.3); 2.3 (95% CI: 1.2-4.4); 1.9 (95% CI: 1.4-2.5); respectively; Figure 2). The association for partial
220 vaccination was less strong and not significant for Beta and Gamma, but still significant for Delta
221 when compared to Alpha (adjusted OR: 1.6 (95% CI: 1.2-2.0); Figure 2). We did not find a significant
222 association between previous infection and the Beta, Gamma or Delta variant over Alpha (adjusted
223 OR: 1.4 (95% CI 0.5-3.7); 0.3 (95%CI 0.0-1.9); 1.0 (95%CI 0.6-1.5), respectively; Figure 2). The Delta
224 variant was significantly associated with younger age groups, which highlights the importance of
225 adjustment for age group (Supplementary Figure 3). When only including data from the genomic
226 surveillance (excluding data from additional sampling of vaccinated and reinfected cases), similar
227 odds ratios were found, although not significant anymore for Beta and Gamma due to less power
228 (data not shown).

229

230 When stratified by vaccine type, the association between full vaccination and infection with the
231 Delta variant was significant for Comirnaty and Janssen COVID-19 vaccine, but not for Spikevax and
232 Vaxzevria (Table 2). The association between partial vaccination and the Delta variant was significant
233 for Comirnaty and Vaxzevria but not Spikevax. In addition, we stratified the fully vaccinated by time
234 since vaccination. The association for individuals with less time (14-59 days) between onset and last

235 dose was higher (OR: 2.3 (95%CI 1.6-3.4)) compared to individuals with 60 days and more (OR: 1.4
236 (95%CI 1.0-2.1)) for the Delta variant. A similar trend was observed for Beta variant and Gamma
237 variant, although with wide confidence intervals (Table 2).

238

239 ***Discussion***

240 Using national epidemiological and whole genome sequencing surveillance data from March to
241 August 2021 in the Netherlands, our analysis provides evidence for an increased risk of infection by
242 the Beta, Gamma, or Delta variants compared to the Alpha variant after full vaccination, regardless
243 of the vaccine used. This indicates lower vaccine effectiveness against infection with the Beta,
244 Gamma and Delta variant compared to the Alpha variant. No clear differences between vaccine type
245 were observed as confidence intervals largely overlap. Interestingly, we did not find a significant
246 difference between susceptibility to any of the investigated VOCs among individuals with immunity
247 due to a previous infection compared to naïve individuals. Also when stratified by time between
248 infections no differences are observed (data not shown). Of note is that these analyses do not aim to
249 determine the probability of getting infected after vaccination or previous infection, but rather
250 calculate the likelihood of getting infected with specific VOCs.

251

252 The association with vaccination status was higher for Beta and Gamma (OR of 3.1 and 2.3,
253 respectively) than for Delta (OR of 1.9), although confidence intervals for Beta and Gamma were
254 wide because of low numbers. This is in line with literature showing lower vaccine effectiveness
255 estimates against infection for Beta and Gamma compared to Delta⁷. An OR for Delta of 1.9
256 implicates a reduction of vaccine effectiveness from 90% to 80%, which has been shown in the
257 UK^{3,27}. Current literature still shows high vaccine effectiveness of 90-95% against severe COVID-19
258 for the Delta variant^{7,17}, which is reassuring. However, note that with very high vaccine effectiveness,
259 a difference of a factor 1.5-2.0 between two variants could go unnoticed, as it would only mean a
260 decrease of effectiveness of 95 to 92%.

261

262 Spike binding and neutralization have been shown to be substantially reduced against Beta, Gamma,
263 and Delta with the largest reduction in neutralization against Beta⁴⁻⁶, which is consistent with our
264 results. This observation did not differ for infection- or vaccine-induced immunity, although
265 convalescent sera from mild infections showed lower levels of neutralization potency to VOCs
266 compared to hospitalized cases and vaccinated individuals⁴. However, in Alpha and Beta a reduction
267 was not observed for T-cell-mediated immunity²⁸.

268

269 We observed a larger effect of vaccination in the first 14-59 days after vaccination (i.e. OR 2.3
270 (95%CI 1.6-3.5) for Delta) compared to 60 days and longer (i.e. OR 1.4 (95%CI 1.0-2.1) for Delta),
271 suggesting that the difference in VE between Delta and Alpha variant reduces over time since
272 vaccination, possibly due to waning immunity. A recent large cohort study describes an effect of
273 waning and a small effect of the circulating variant (i.e. Delta vs non-Delta) on the VE against SARS-
274 CoV-2 infection²⁹. They find a non-delta VE of 97% and a delta VE of 93% one month after
275 vaccination, which means a ratio of 2.3 between non-delta VE and delta VE. Four to five months post
276 vaccination, VE estimates of 67% and 53% for non-delta and delta were observed respectively, a
277 ratio of 1.4. This very well corresponds with our results. Given the broad and sometimes overlapping
278 confidence intervals of these data, however, the differences need to be interpreted with caution.

279

280 We found no association between previous infection and a new infection with Beta, Gamma or Delta
281 versus Alpha, suggesting that there is a no difference in immunity between Alpha and Beta, Gamma
282 or Delta after previous infection, in contrast to vaccine-induced immunity. It is not yet clear whether
283 previous infection or vaccination induces better protection against infection. However, primary
284 infection comes with a risk of hospitalization or death, especially in older persons or individuals with
285 underlying conditions. Even if infection-induced immunity protects better against reinfection with

286 novel variants, vaccination is preferred over infection to protect individuals against severe disease as
287 the cumulative risk from two infections should be taken into account.

288

289 Some limitations of our study need to be addressed. Asymptomatic or mild cases with low viral load
290 are less likely to be identified and only detectable infections can be sequenced and included. In
291 addition, sequencing is more successful in samples with low to medium Ct values (high to medium
292 viral load). If infection with Beta, Gamma or Delta leads to lower Ct values than Alpha and Ct values
293 are higher for infections after vaccination³⁰⁻³², this could have led to an overestimation of the
294 studied association. Another limitation is that prior infections could go undetected, especially if
295 occurred during the first wave when there was no mass scale testing capacity. This could lead to an
296 underestimation of cases with a previous infection, as we do not directly measure pre-existing
297 infection-induced immunity.

298

299 In conclusion, our results confirm a lower vaccine effectiveness against infection for the Delta
300 variant, and similarly the Beta and Gamma variant, compared to Alpha. This effect was largest early
301 after complete vaccination. These findings are informative for considerations on vaccine updates,
302 future vaccination and pandemic control strategies.

303

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306 the national surveillance database and all laboratories for providing specimens for sequence
307 analyses.

308

309 *Code availability*

310 Code for sequencing data processing is publicly available at [github.com/RIVM-](https://github.com/RIVM-bioinformatics/SARS2seq)
311 [bioinformatics/SARS2seq](https://github.com/RIVM-bioinformatics/SARS2seq). Scripts for statistical analysis, figures, and tables can be found at
312 github.com/Stijn-A/xxxxx. [upon publication]

313

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394 **Figures and Tables**

395

396 **Figure 1** Variants found in SARS-CoV-2 positive samples of individuals with naïve (unvaccinated and
397 no known previous infection), vaccine-induced, or infection-induced immune status. Number of naïve,
398 partly vaccinated, fully vaccinated, and reinfected documented SARS-CoV-2 positive individuals by
399 variant from March 1 to August 31, 2021 (upper panel) and proportion of the respective groups
400 (lower panel).

401

402 **Figure 2** Odds ratios of the logistic regression models for the association between immune status and
403 VOC (Beta, Gamma or Delta over the Alpha variant) adjusted for week of sampling, sex and 10-year
404 age group. Error bars correspond to the 95% confidence intervals.

405

406 **Table 1** Characteristics of notified SARS-CoV-2 positive cases overall and for which variant
407 information was available, 1 March to 31 August 2021, the Netherlands

	Notifications	Variant information from genomic surveillance	Variant information from additional sampling
Total	661,658	29,305	1,516
Immune status			
Naïve	487,063 (73.6%)	20,804 (71.0%)	NA
Recently vaccinated	47,565 (7.2%)	2,140 (7.3%)	18 (1.2%)
Partly vaccinated	38,261 (5.8%)	2,016 (6.9%)	707 (46.6%)
Fully vaccinated	25,933 (3.9%)	1,791 (6.1%)	516 (34.0%)
Previous infection	10,565 (1.6%)	284 (1.0%)	191 (12.6%)
Vaccinated and previous infection	2,065 (0.3%)	62 (0.2%)	49(3.2%)
Unknown	50,206 (7.6%)	2,208 (7.5%)	35 (2.3%)
Age group			
0-9	42,666 (6.4%)	1,818 (6.2%)	4(0.3%)
10-19	125,782 (19.0%)	5,869 (20.0%)	111 (7.3%)
20-29	157,896 (23.9%)	7,018 (23.9%)	283 (18.7%)
30-39	92,400 (14.0%)	4,162 (14.2%)	187 (12.3%)

40-49	85,492 (12.9%)	3,851 (13.1%)	222 (14.6%)
50-59	87,112 (13.2%)	3,652 (12.5%)	265 (17.5%)
60-69	44,226 (6.7%)	1,828 (6.2%)	251 (16.6%)
70-79	21,074 (3.2%)	848 (2.9%)	86 (5.7%)
80+	5,010 (0.8%)	259 (0.9%)	107 (7.1%)
Sex			
Male	330,247 (49.9%)	14,437 (49.3%)	629 (41.5%)
Female	331411 (50.1%)	14,868 (50.7%)	692 (58.5%)
Symptoms			
Yes	556,214 (84.1%)	25,478 (86.9%)	1355 (89.4%)
No	66,593 (10.1%)	2,248 (7.7%)	121 (8.0%)
Unknown	38,851 (5.9%)	1,579 (5.4%)	40 (2.6%)
Month (sampling date)			
March	149,103 (22.5%)	5,408 (18.5%)	177 (11.7%)
April	171,534 (25.9%)	4,621 (15.8%)	335 (22.1%)
May	114,536 (17.3%)	4,874 (16.6%)	137 (9.1%)
June	24,904 (3.8%)	3,162 (10.8%)	97 (6.4%)
July	146,978 (22.2%)	6,620 (22.6%)	438 (28.9%)
August	54,603 (8.3%)	4,620 (15.8%)	331(21.8%)

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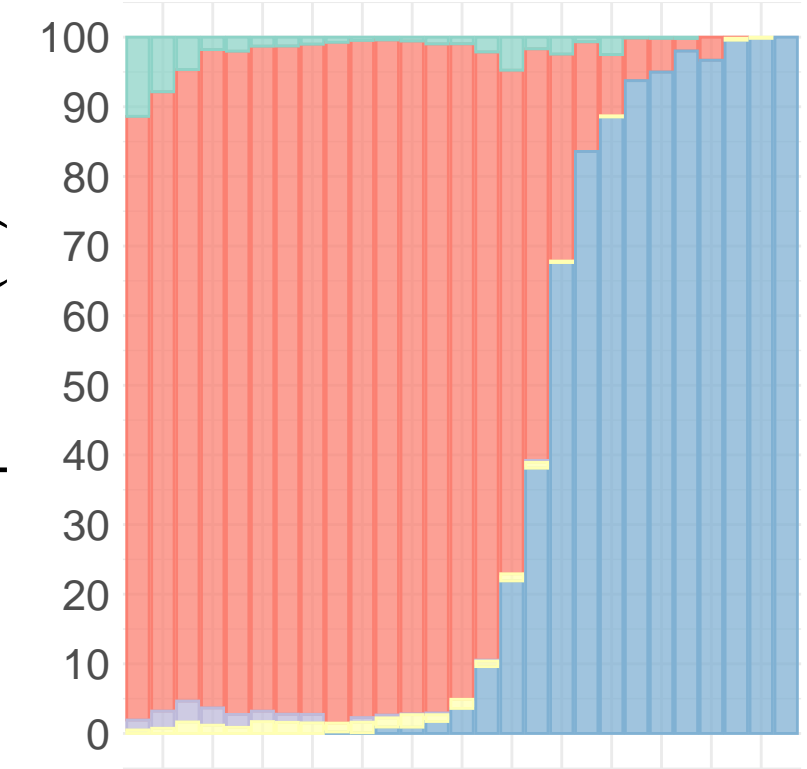
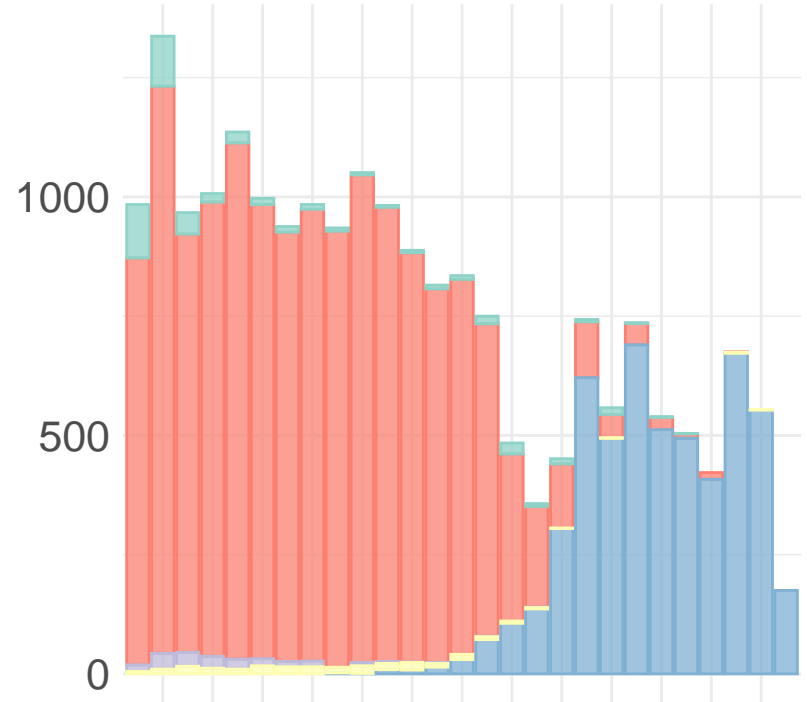
411 **Table 2** Odds ratios (ORs) and 95% confidence intervals (CIs) for the association between immune
412 status and VOC (Beta, Gamma or Delta over the Alpha variant) by vaccine type and days between
413 onset and last dose, both adjusted for week of sampling, sex and 10-year age group.

	Beta	Gamma	Delta
	OR (95% CI)	OR (95% CI)	OR (95% CI)
Naïve	Reference	Reference	Reference
Partly vaccinated			
Comirnaty	1.1 (0.3-3.7)	1.9 (1.0-3.7)	1.8 (1.4-2.3)
Spikevax	n/a	2.5 (0.6-10.4)	1.1 (0.6-2.0)
Vaxzevria	2.1 (1.0-4.1)	1.0 (0.5-2.0)	2.1 (1.3-3.5)
Fully vaccinated			
Comirnaty	3.2 (1.4-7.7)	2.2 (1.0-4.7)	2.2 (1.4-3.3)
Spikevax	n/a	n/a	1.3 (0.4-4.3)
Vaxzevria	n/a	2.8 (0.7-12.3)	1.4 (0.9-2.3)
Janssen	n/a	4.4 (0.6-34.5)	2.2 (1.2-4.2)
Naïve	Reference	Reference	Reference
Fully vaccinated			
14-60 days	3.7 (1.4-9.5)	3.0 (1.3-7.1)	2.3 (1.6-3.4)
>60 days	1.7 (0.2-12.8)	1.7 (0.6-4.6)	1.4 (1.0-2.1)

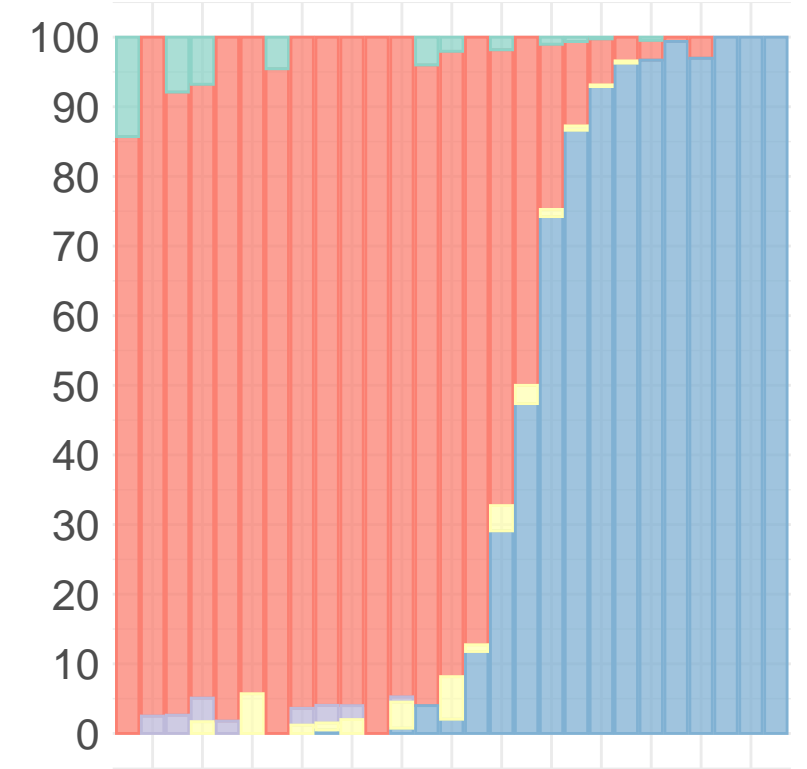
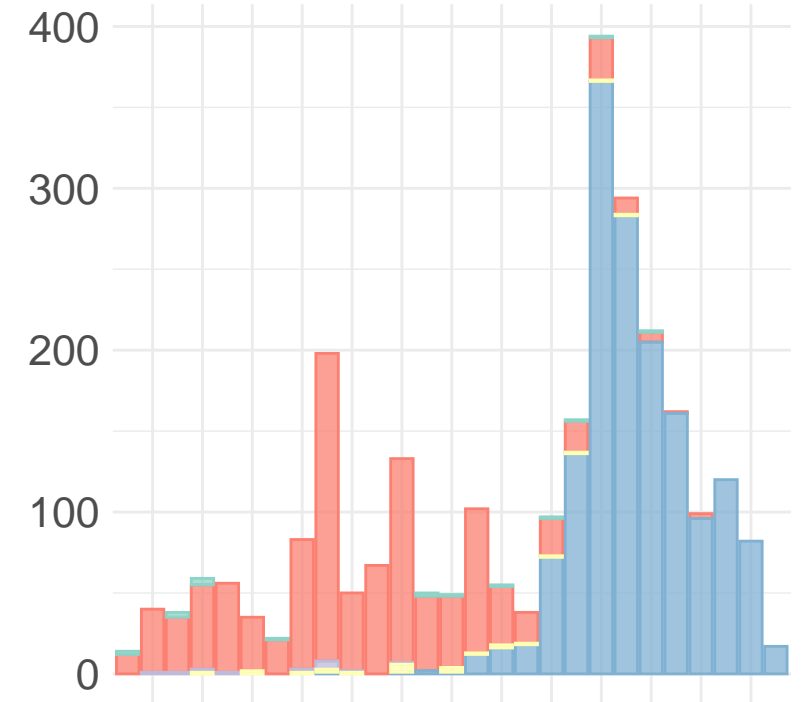
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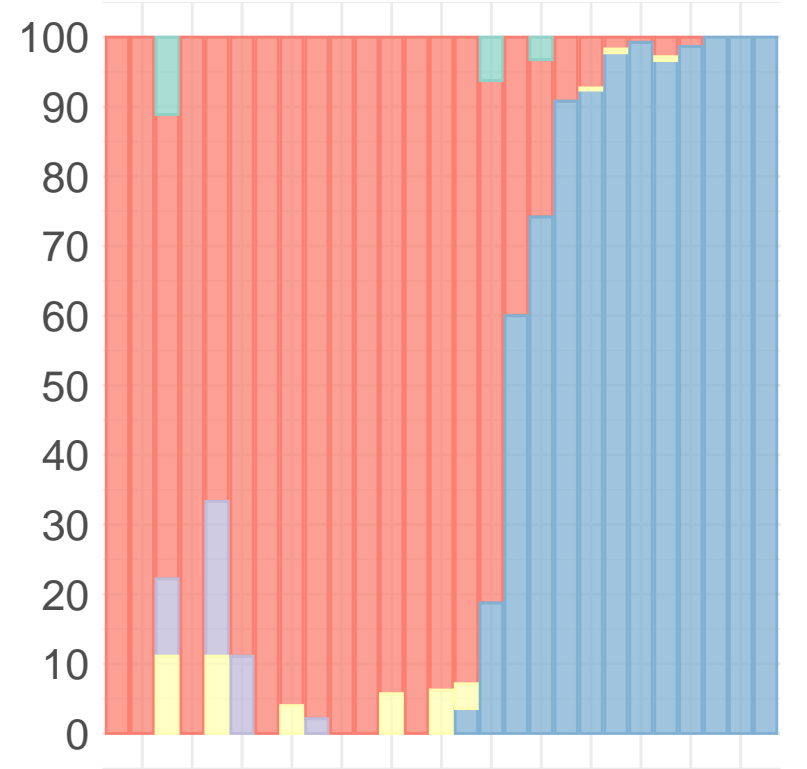
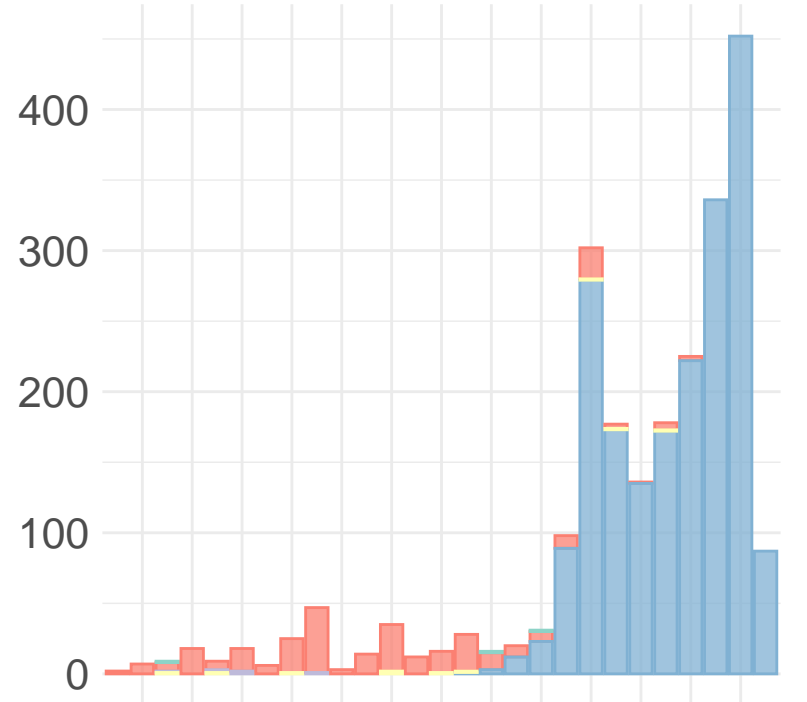
Naive



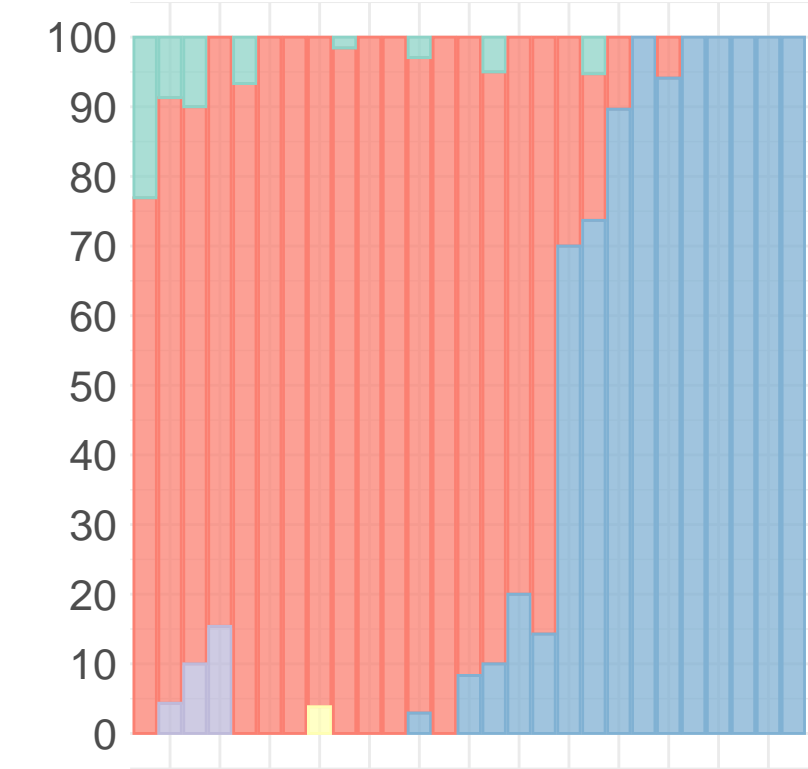
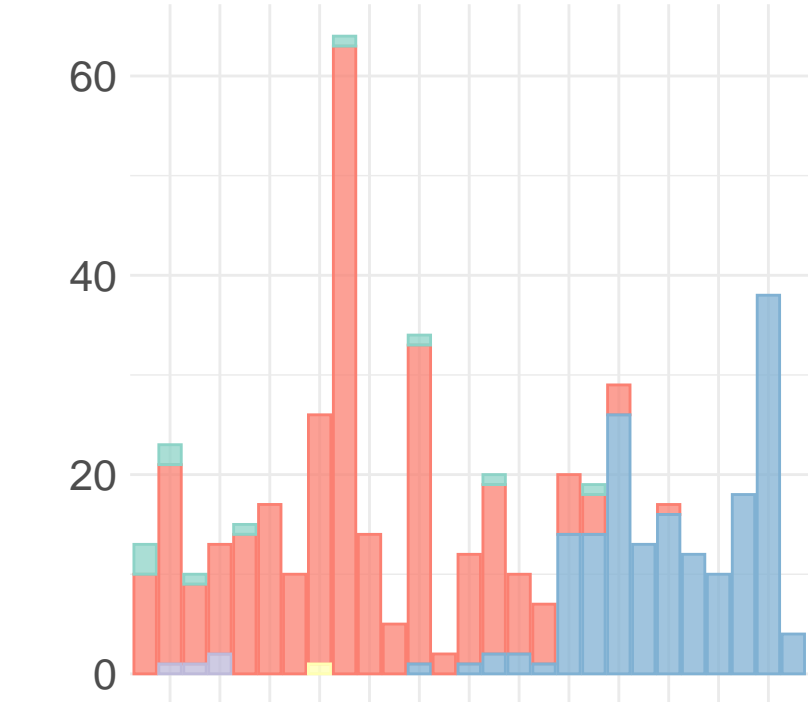
Partly vaccinated



Fully vaccinated



Previous infection



Sampling ISOweek

