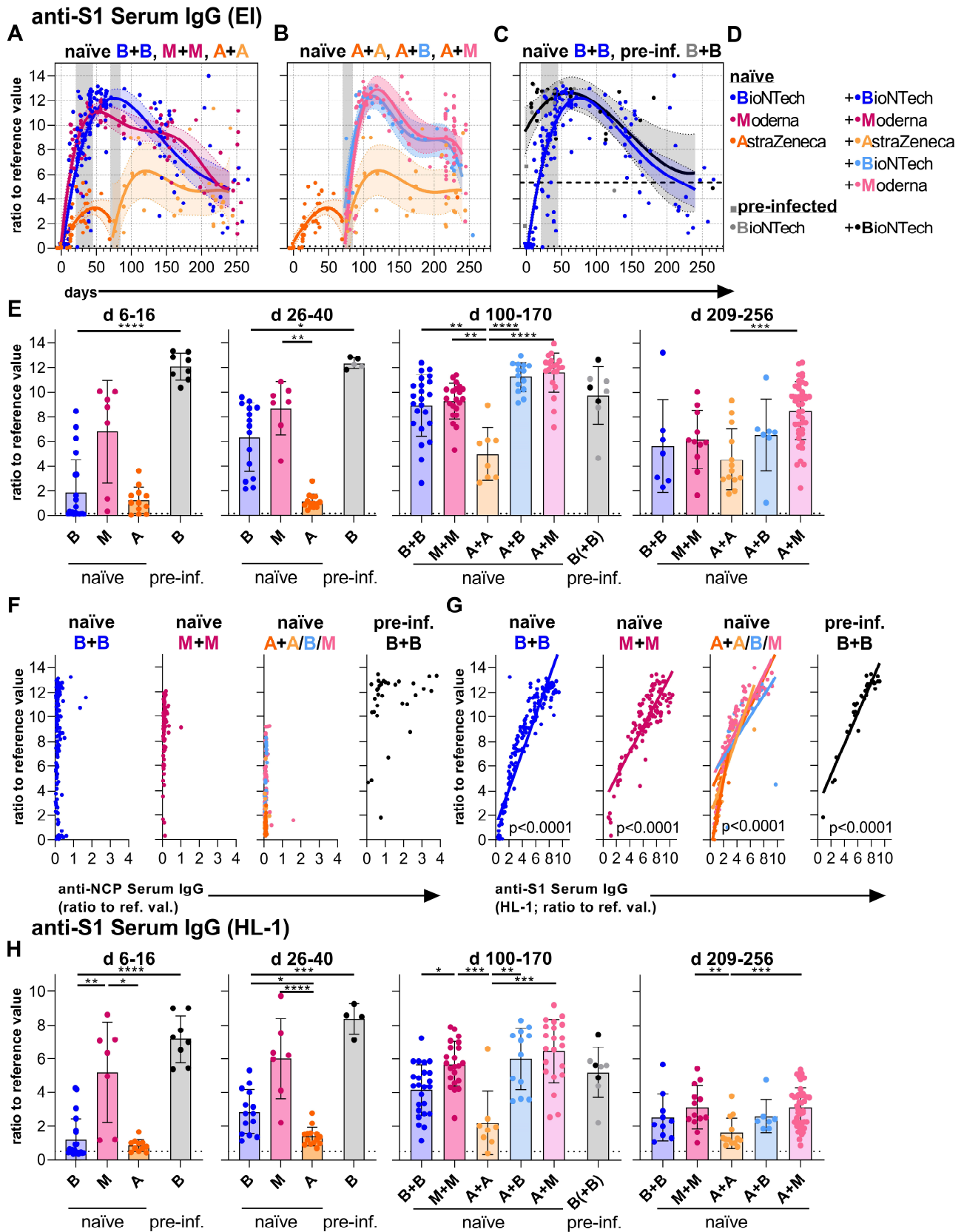
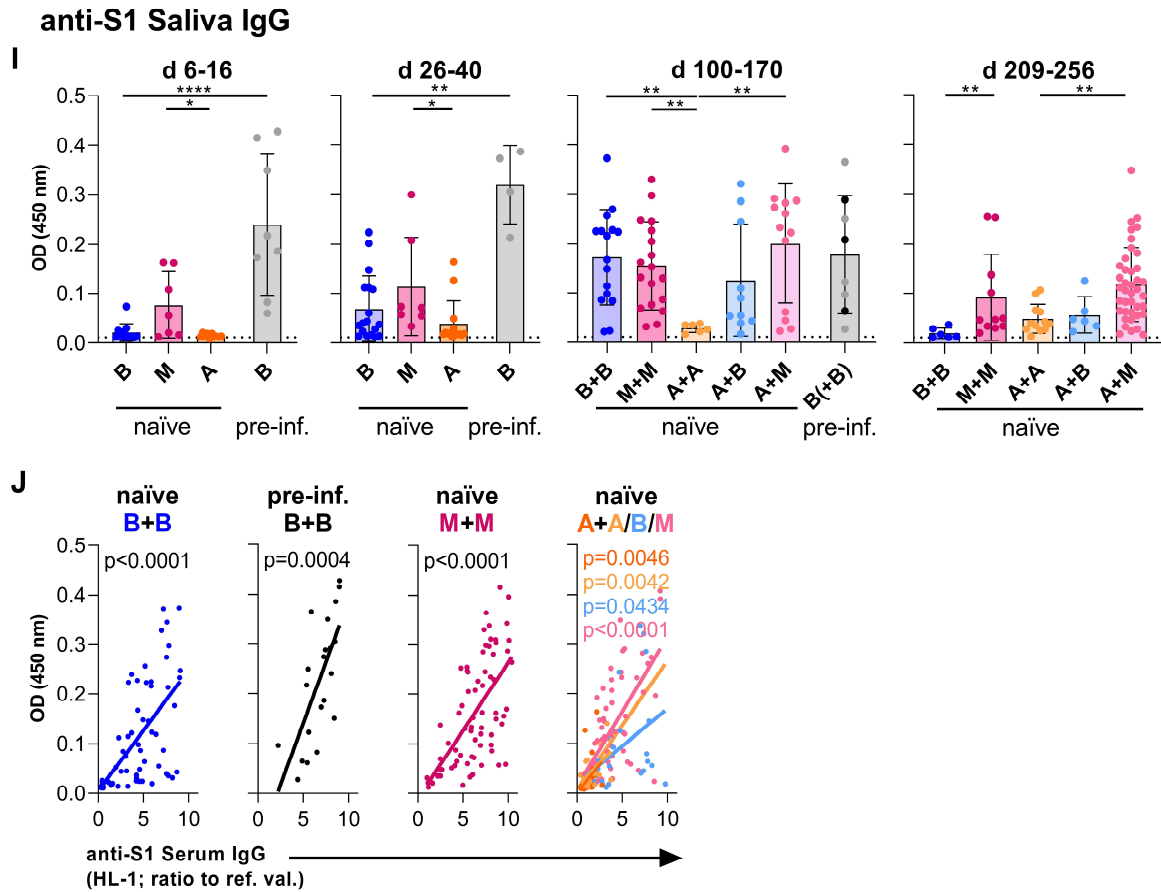


## Supplementary Material



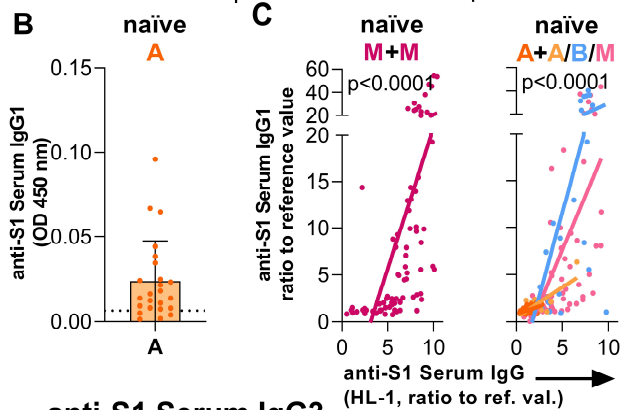
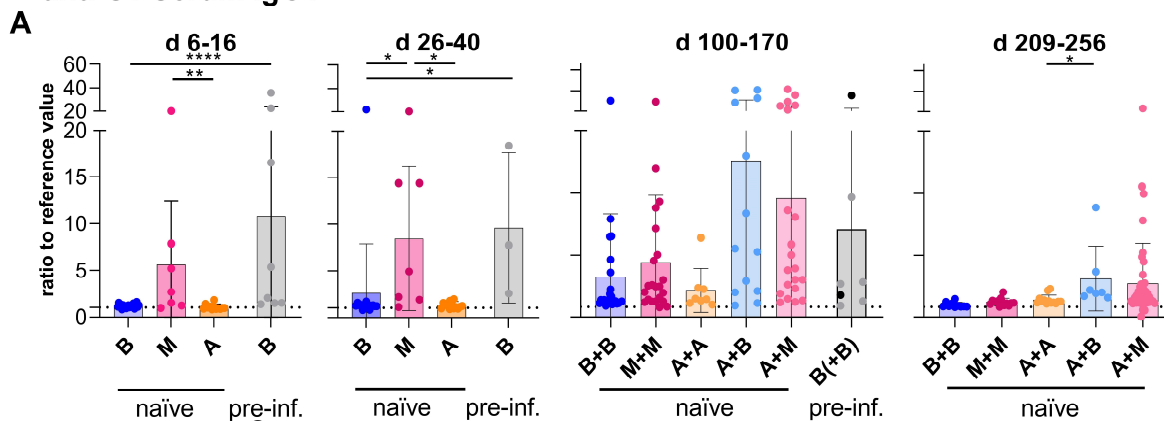


**Fig. S1. Anti-S1 serum and saliva IgG levels.**

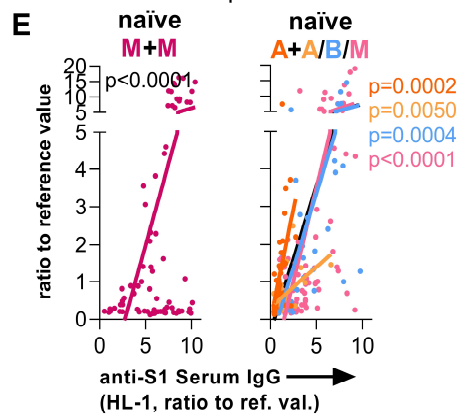
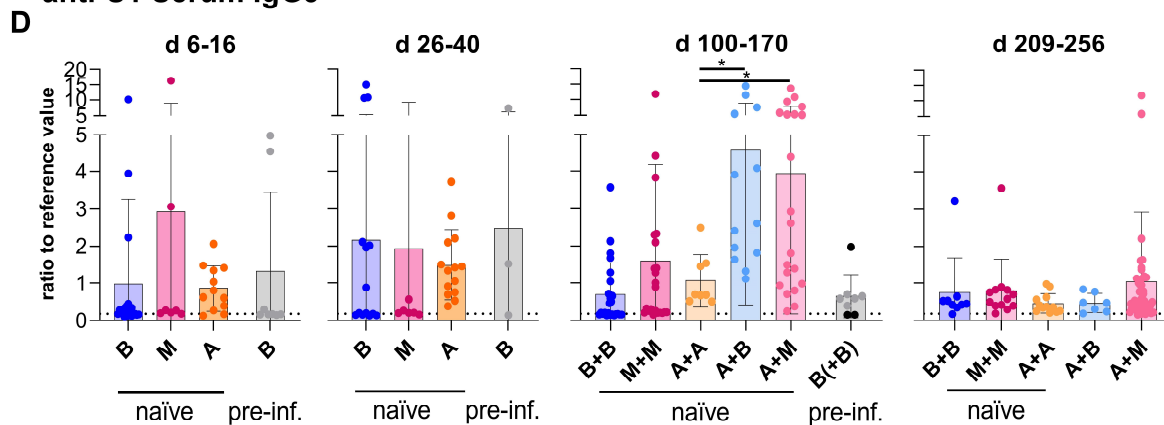
(A-C) Anti-S1 serum IgG (EUROIMMUN (EI) ELISA) levels (ratio to reference values) of the indicated six vaccination groups. Gray bars: time windows of the second shot after the first shot with an mRNA (between day 21 and 45) or adenovirus-based (between day 70 and 84) vaccine. (D) Color legend of all six groups. (E) Anti-S1 serum IgG (EI ELISA) levels (the same y-axis as in (A)) of the six indicated groups for four different time intervals (data points from A-C). All samples of the second time interval (days 26-40) were taken before the second vaccination. Dashed (C) and dotted lines indicate the corresponding anti-S1 IgG average levels of pre-infected individuals without/ before vaccination or non-vaccinated healthy (negative) controls. (F) Correlations between anti-NCP serum IgG levels (ratio to reference value) and anti-S1 serum IgG (EI ELISA) levels (the same y-axis as in (A) and (E)) of the indicated groups. (G) Correlations between anti-S1 serum IgG (HL-1 ELISA) levels (data points from **Fig. 1A-C**) and anti-S1 serum IgG (EI ELISA) levels (the same y-axis as in (A), (E), and (F)) of the indicated groups.  $p$ -values of the indicated correlations are shown (the  $p$ -values for the naïve A+A/B/M groups are the same). (H) Anti-S1 serum IgG (HL-1 ELISA) levels of the indicated six groups for four different time intervals (data points from **Fig. 1A-C**). (I) Anti-S1 saliva IgG levels of the indicated six groups for four different time intervals (data

points from **Fig. 1E-G**). **(J)** Correlations between anti-S1 serum IgG (HL-1 ELISA) levels and anti-S1 saliva IgG levels. The same y-axis as in **(I)** and **Fig. 1E**. Statistics: Mann-Whitney test for the comparison of naïve and pre-infected (B(+B) vaccinees; Kruskal-Wallis test for the comparison of all naïve groups.

## anti-S1 Serum IgG1



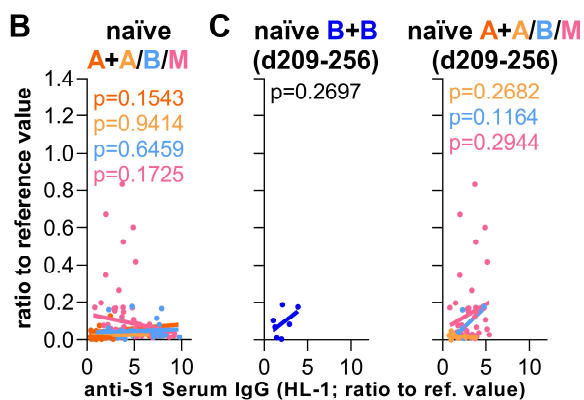
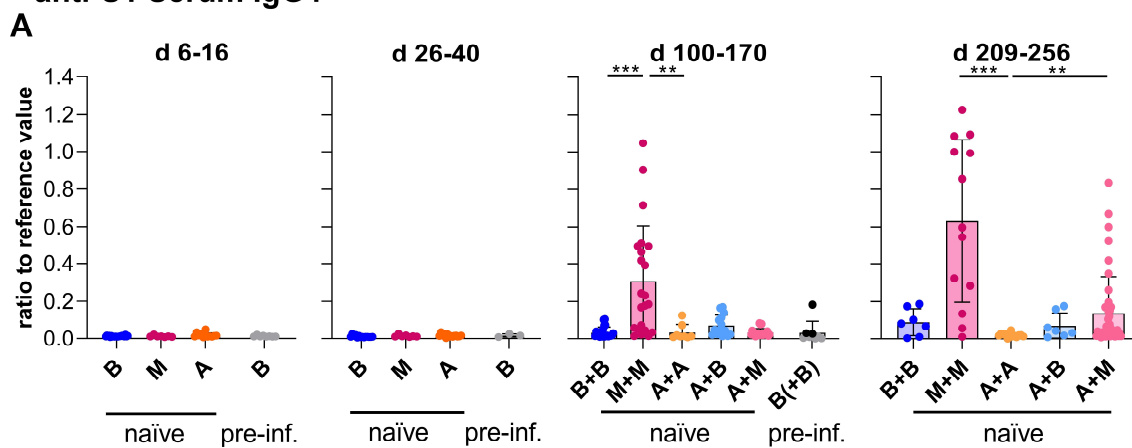
## anti-S1 Serum IgG3



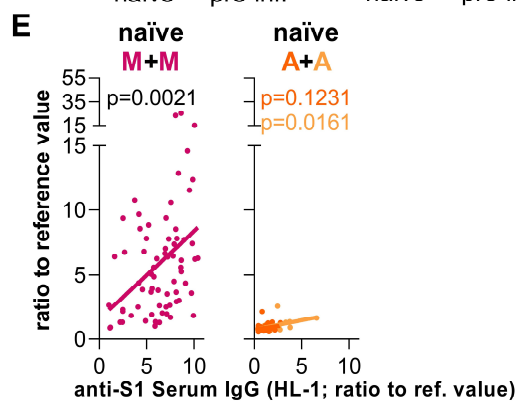
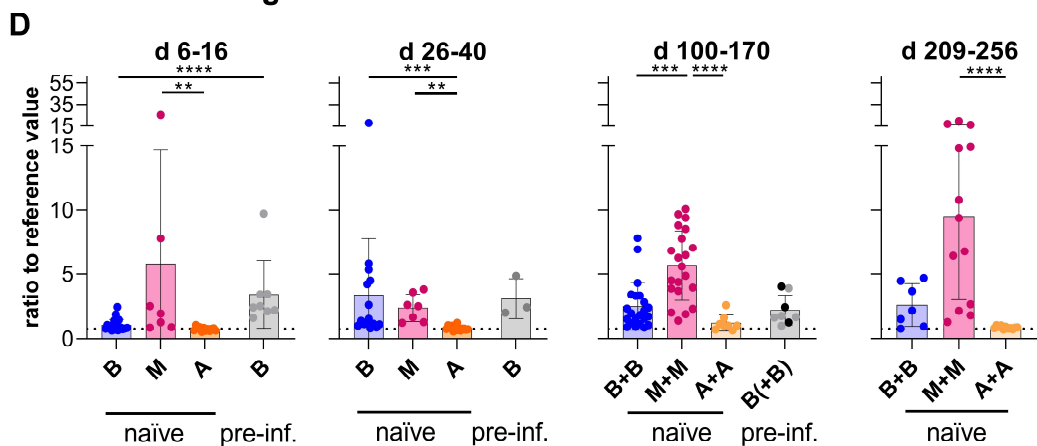
**Fig. S2. Anti-S1 serum IgG1 and IgG3 subclass levels.**

(A) Anti-S1 serum IgG1 levels of the indicated six vaccination groups for four different time intervals (data points from **Fig. 2**). All samples of the second time interval (days 26-40) were taken before the second vaccination. (B) Anti-S1 serum IgG1 ELISA (OD 450 nm) data for individuals immunized one-time with AZD1222 (serum dilution 1/10). (C) Correlations between anti-S1 serum IgG (HL-1 ELISA) levels and anti-S1 serum IgG1 levels (extension to correlations in **Fig. 2**). *p*-values of the indicated correlations are shown (the *p*-values for naïve A+A/B/M groups are the same). (D) Anti-S1 serum IgG3 levels of the indicated six groups for four different time intervals (data points from **Fig. 2**). (E) Correlations between anti-S1 serum IgG (HL-1 ELISA) levels and anti-S1 serum IgG3 levels (extension to correlations in **Fig. 2**). Dotted lines indicate the corresponding anti-S1 IgG1 or 3 average levels of non-vaccinated healthy (negative) controls. Statistics: Mann-Whitney test for the comparison of naïve and pre-infected (B(+B) vaccinees; Kruskal-Wallis test for the comparison of all naïve groups.

## anti-S1 Serum IgG4

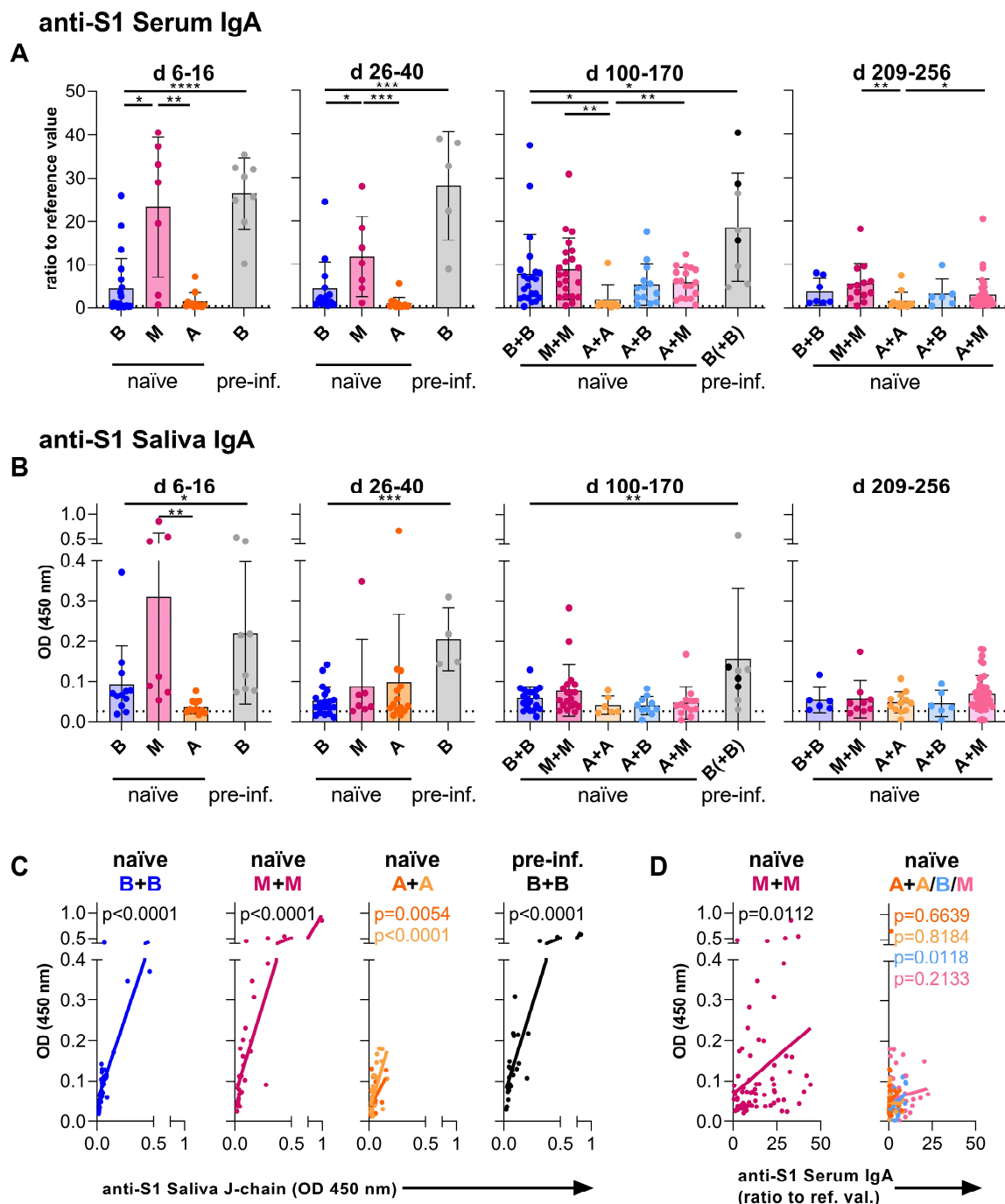


## anti-S1 Serum IgG2



**Fig. S3. Anti-S1 serum IgG4 and IgG2 subclass levels.**

(A) Anti-S1 serum IgG4 levels of the indicated four groups for four different time intervals (data points from **Fig. 2**). All samples of the second time interval (days 26-40) were taken before the second vaccination. (B) Correlations between anti-S1 serum IgG (HL-1 ELISA) levels and anti-S1 serum IgG4 levels (extension to correlations in **Fig.2**). *p*-values of the indicated correlations are shown. (C) Correlations between anti-S1 serum IgG (HL-1 ELISA) levels and anti-S1 serum IgG4 levels between day (d) 209-256 (extension to correlations in **Fig. 2**). (D) Anti-S1 serum IgG2 levels of the indicated four groups for four different time intervals (data points from **Fig. 2**). (E) Correlations between anti-S1 serum IgG (HL-1 ELISA) levels and anti-S1 serum IgG2 levels (extension to correlations in **Fig. 2**). Dotted lines indicate the corresponding anti-S1 IgG2 or 4 average levels of non-vaccinated healthy (negative) controls. Statistics: Mann-Whitney test for the comparison of naïve and pre-infected B(+B) vaccinees; Kruskal-Wallis test for the comparison of all naïve groups.

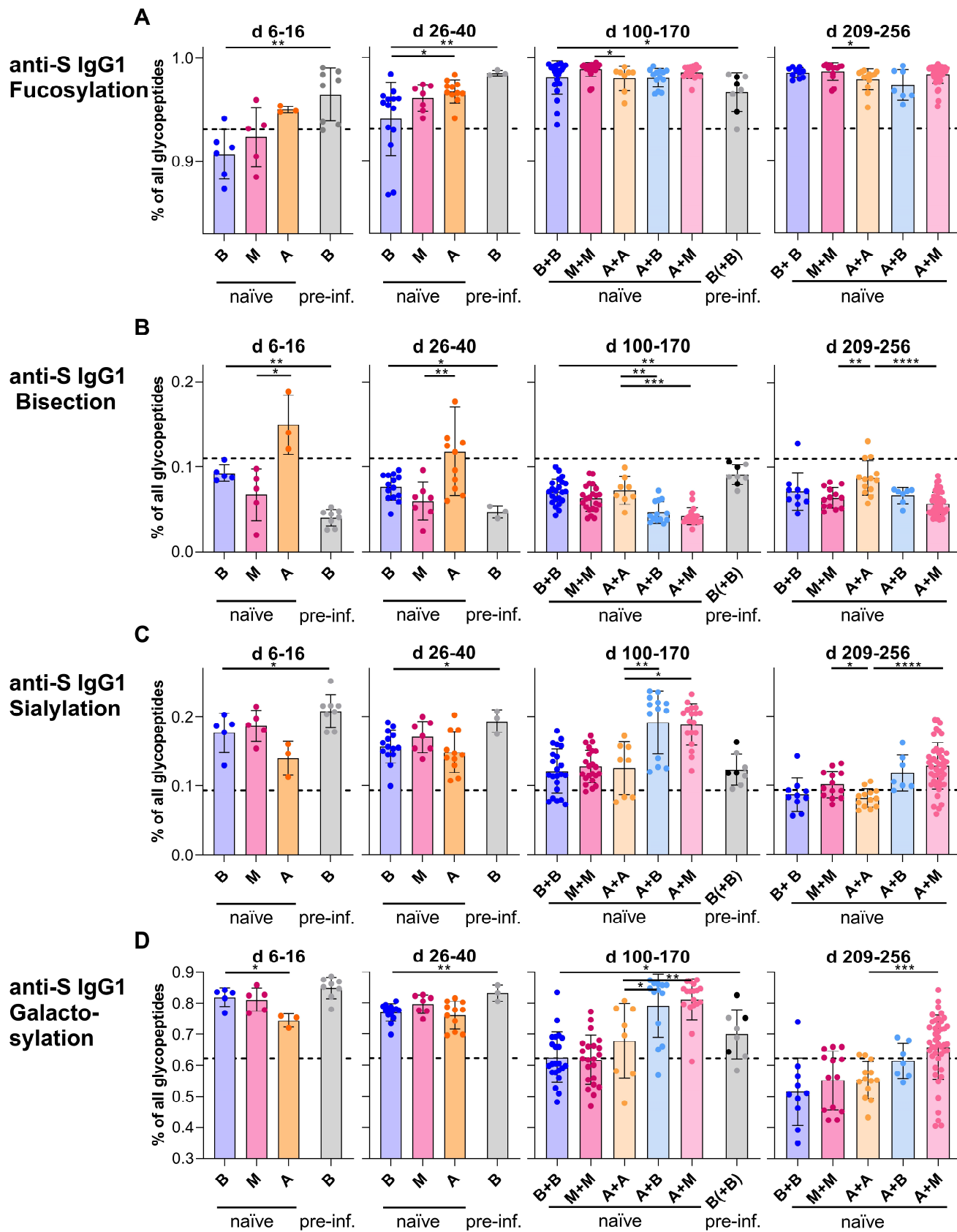


**Fig. S4. Anti-S1 serum and saliva IgA levels.**

(A and B) Anti-S1 (A) serum and (B) saliva IgA levels of the indicated six vaccination groups for four different time intervals (data points from **Fig. 3**). All samples of the second time interval (days 26-40) were taken before the second vaccination. Dotted lines indicate the corresponding anti-S1 serum or saliva IgA average levels of non-vaccinated healthy (negative) controls. (C) Correlations between anti-S1 saliva J-chain and anti-S1 saliva IgA levels. (D) Correlations between anti-S1 serum IgA and anti-S1 saliva IgA levels (extension to correlations

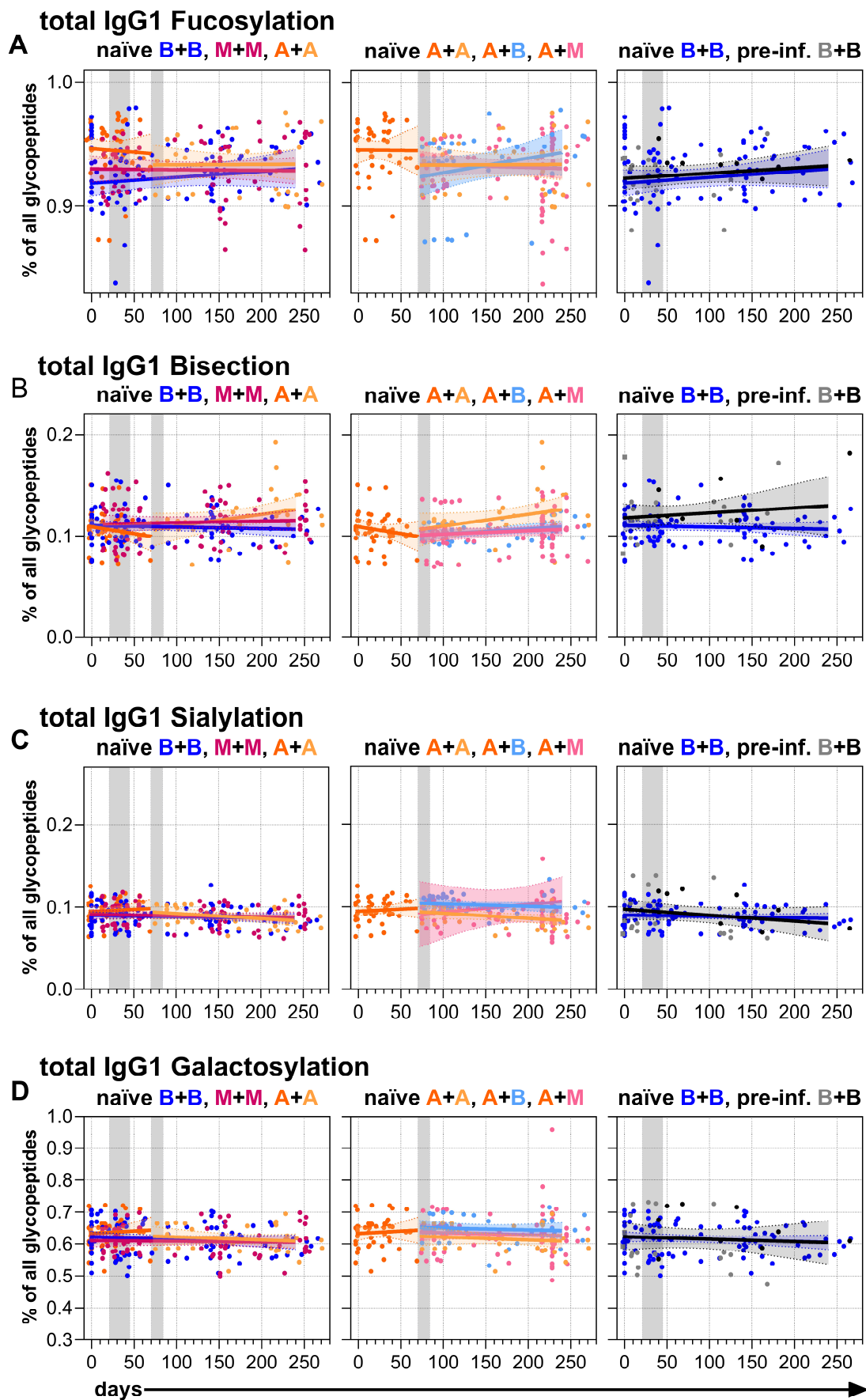


in **Fig. 3**) of the indicated groups.  $p$ -values of the indicated correlations are shown. Statistics: Mann-Whitney test for the comparison of naïve and pre-infected B(+B) vaccinees; Kruskal-Wallis test for the comparison of all naïve groups.



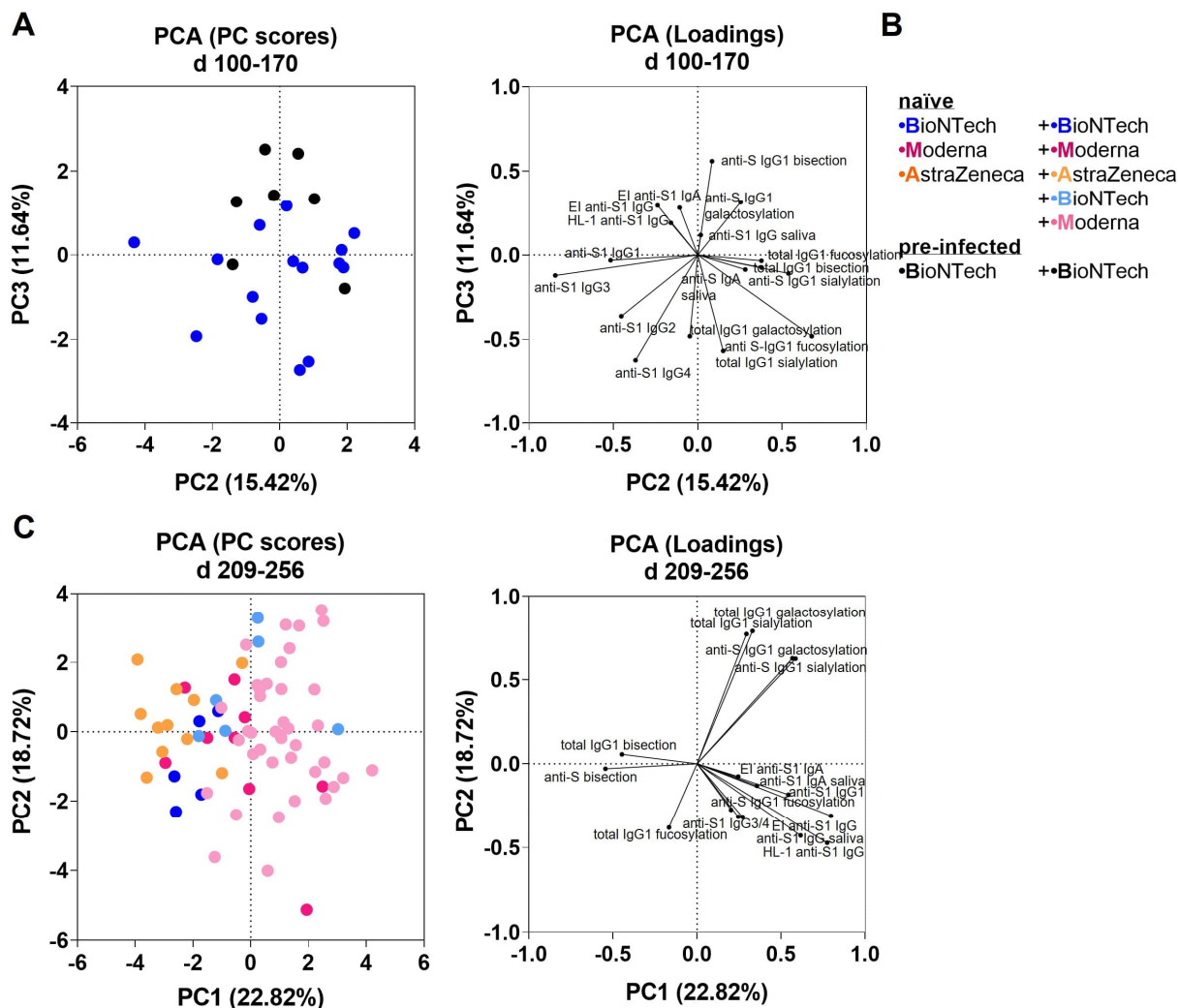
**Fig. S5. Anti-S1 serum IgG1 Fc *N*-glycosylation**

(**A-D**) Anti-S serum IgG1 Fc *N*- (A) fucosylation, (B) bisection, (C) sialylation, and (D) galactosylation of the indicated six vaccination groups for four different time intervals (data points from **Figs. 4 and 5**). All samples of the second time interval (days 26-40) were taken before the second vaccination. Dashed lines indicate the average level of total IgG1 Fc *N*-fucosylation, bisection, sialylation, or galactosylation, respectively (**Fig. S6**). Statistics: Mann-Whitney test for the comparison of naïve and pre-infected B(+B) vaccinees; Kruskal-Wallis test for the comparison of all naïve groups.



**Fig. S6. Total serum IgG1 Fc *N*-glycosylation**

(**A-D**) Total serum IgG1 Fc *N*- (A) fucosylation, (B) bisecting, (C) sialylation, and (D) galactosylation for the indicated six vaccination groups. The color legend is shown in **Fig. 1D**. Gray bars: time windows for the second shot after the first shot with an mRNA (between day 21 and 45) or adenovirus-based (between day 70 and 84) vaccine.



**Fig. S7. Principal component analysis (PCA).**

(A) PCA of data collected from naïve and pre-infected B(+B) vaccinated individuals between day (d) 100 and 170 upon first vaccination. Loadings as well as PC scores are shown. (B) Colour coding of all six vaccination groups. (C) PCA of data from all naïve vaccinated individuals between day 209 and 256 upon first vaccination.

**Table S1: Age- and sex-distributions of all vaccination groups.**

group→ variable↓	Naïve BioNTech/Pfizer + BioNTech/Pfizer	Naïve Moderna + Moderna	Naïve AstraZeneca + AstraZeneca	Naïve AstraZeneca + BioNTech	Naïve AstraZeneca + Moderna	Pre-infected BioNTech/Pfizer + BioNTech/Pfizer
<b>Age (years)</b>						
Average (Min- Max)	$\bar{X}$ 36 (19-66)	$\bar{X}$ 42 (22-61)	$\bar{X}$ 41 (22-62)	$\bar{X}$ 30 (23-44)	$\bar{X}$ 36 (22-63)	$\bar{X}$ 47 (27-74)
<b>Sex at Birth</b>						
Female	26	21	7	9	33	8
Male	22	4	7	3	11	6
Both	48	25	14	12	44	14

**Table S2: IgG1 glycopeptides included in the final analyte list.** Shown are the compositions, IgG glycan names according to alternative nomenclature, the monoisotopic mass of detected glycan species in the 2+ and 3+ charge, and proposed structures. The position and linkage of monosaccharides are proposed based on literature. In the glycan composition column, H: hexose; N: N-acetylhexosamine; F: fucose; S: N-acetylneuraminic acid (sialic acid).

Glycan composition	Alternative nomenclature	m/z [M+2H] <sup>2+</sup>	m/z [M+3H] <sup>3+</sup>	Proposed structure	Mean (of total IgG1 analysis)	SD (+/-)	Compositions of hospitalized patients; raw glycopeptide peak data identified in the context of our previous study (60) that were used for calculation
H3N4F1	G0F	1317.527	878.687		<b>16.32</b>	4.40	x
H4N4	G1	1325.524	884.018		3.02	1.35	x
H4N4F1	G1F	1398.553	932.704		<b>30.36</b>	2.73	x
H5N4	G2	1406.550	938.036		2.06	0.91	
H5N4F1	G2F	1479.579	986.722		<b>21.08</b>	2.56	x
H4N5F1	G1FN	1500.093	1000.398		<b>8.24</b>	1.34	x
H4N4F1S1	G1FS1	1544.101	1029.736		2.04	0.29	x
H5N4S1	G2S1	1552.098	1035.068		1.33	0.51	x
H5N5F1	G2FN	1581.119	1054.415		2.15	0.65	
H5N4F1S1	G2FS1	1625.127	1083.754		<b>12.54</b>	2.77	x
H5N5F1S1	G2FNS1	1726.668	1151.447		0.43	0.13	x
H5N4F1S2	G2FS2	1770.675	1180.786		0.43	0.13	x
<b>sum</b>					100%		100%



**Table S3: Description and calculation of IgG1 glycosylation traits.**

<b>Derived trait</b>	<b>Description</b>	<b>Formula</b>
<b>fucosylation</b>	<i>N</i> -glycans carrying a core fucose	$( H3N4F1 + H4N4F1 + H5N4F1 + H4N5F1 + H5N5F1 + H4N4F1S1 + H5N4F1S1 + H5N4F1S2 + H5N5F1S1 ) / \text{sum of all glycopeptides}$
<b>bisection</b>	<i>N</i> -glycans carrying a bisected <i>N</i> -acetylglucosamine	$( H4N5F1 + H5N5F1 + H5N5F1S1 ) / \text{sum of all glycopeptides}$
<b>galactosylation</b>	<i>N</i> -glycans carrying a galactose	$( 1/2 * (H4N4 + H4N4F1 + H4N5F1 + H4N4F1S1) + 2/2 * (H5N4 + H5N4F1 + H5N5F1 + H5N4S1 + H5N4F1S1 + H5N4F1S2 + H5N5F1S1) ) / \text{sum of all glycopeptides}$
<b>sialylation</b>	<i>N</i> -glycans carrying an <i>N</i> -acetylneuraminic acid (sialic acid)	$( 1/2 * (H5N4S1 + H4N4F1S1 + H5N4F1S1 + H5N5F1S1) + 2/2 * H5N4F1S2 ) / \text{sum of all glycopeptides}$