# Previous immunity shapes immune responses to SARS-CoV-2 booster vaccination and Omicron breakthrough infection risk

# Supplementary Information

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## Supplementary Methods

### 1. Extended experimental methodology

#### 1.1. Estimation of anti-receptor-binding domain (RBD) antibody levels

Quantitative estimation of circulating levels of IgG and IgA against ancestral S protein receptor-binding domain (RBD) was evaluated using a national-validated in-house developed ELISA-based assay previously described[1]. Shortly, in-house produced recombinant RBD was coated onto Nunc-Maxisorp 384-well plates (Thermo Fisher Scientific) overnight at 4 ℃ (1 µg/ml in PBS). The plates were blocked using PBS + 0.05% Tween (Merck) (PBS-T) for 1 hour. Serum samples were diluted accordingly and applied in PBS-T + 5mM EDTA and incubated for 1 hour. RBD-bound antibodies were detected using 0.5 µg/ml HRP-conjugated polyclonal rabbit anti-IgG or IgA (both from Agilent Technologies) and incubated for 1 hour. TMB-One (Kem-En-Tec) was used as a substrate to reveal the plates for 7 min and 10 min for IgG and IgA, respectively. The reaction was stopped by adding 0.3 M $H_2SO_4$. The calibrator used was a combination of equal concentrations of recombinant human IgG and IgA antibodies against S protein/RBD (1:2000 dilution, both from Genscript). Finally, optical density was measured at 450-630 nm using a Synergy HT absorbance reader (Biotek Instruments). Otherwise stated, all incubations were performed at room temperature shaking. PBS-T was used as washing buffer four times between incubation steps. The threshold for assay positivity was set to 200 and 100 AU/ml for IgG and IgA, respectively, with a sensitivity and specificity of 94.3% and 99.5% and 63.4% and 99.3% for IgG and IgA, respectively[1].

#### 1.2. ACE-2/RBD antibody inhibition quantification

Using an in-house developed pseudo-neutralization ELISA-based assay we estimated the inhibitory capacity of circulating antibodies to prevent the interaction between the host receptor ACE-2 and RBD, as previously described[2]. Briefly, recombinant ACE-2 produced in-house was coated onto Nunc Maxisorp 96-well plates (Thermo Fisher Scientific) overnight at 4 ℃ (1 µg/ml in PBS). In Nunc low-binding round-bottom 96-well plates (Thermo Fisher Scientific) serum samples were diluted accordingly and co-incubated with a solution containing HRP-conjugated high-sensitivity streptavidin (dilution 1:16000, Pierce) and biotinylated recombinant RBD (4 ng/ml, in-house produced) in PBS-T for 1 hour. Following this, the mixture was transferred to the ACE-2-coated plates and incubated for 35 minutes. The plates were developed for 20 min as described above. Otherwise stated, all incubations were performed at room temperature shaking. PBS-T was used as washing buffer four times between incubation streps. The threshold for assay positivity was set to 420 IU/ml with a sensitivity and specificity of 99.5% sensitivity and 98.8% specificity. This pseudo-

neutralizing assay has a great correlation (r=0.9231) with the gold standard plaque reduction neutralization test[2].

### 1.3. T-cell stimulation and IFN-γ quantification

T-cells in whole blood were specifically stimulated with S1-based peptides using the SARS-CoV-2 IGRA stimulation tube set from EUROIMMUN (ET 2606-3003) following manufacturer's instructions. Shortly, heparinized whole blood (0.5 ml) was aliquoted into the stimulation tubes provided by the kit: a) a blank tube to quantify the unspecific stimulation of T-cells and subsequent IFN-γ release, b) a specific tube containing S1-based peptides, and c) a positive tube containing a mitogen. Tubes containing blood were inverted six times and incubated for 21 hours at 37 ℃. Thereafter, the reaction was stopped by centrifugation at 12,000 g for 10 min. The plasma mas collected and stored (- 80 ℃) until quantification of IFN-γ released.

IFN-γ released from T-cells upon stimulation was quantified using the IFN-γ ELISA kit from EUROIMMUN (ET 6841-9601) following manufacturer's instructions. Shortly, diluted samples were applied into the pre-coated plates in sample buffer and incubated for 2 hours. The standard curve and the controls provided by the kits were applied undiluted. Bound IFN-γ was detected by incubating for 30 minutes a biotin-labeled antibody against human IFN-γ followed by 30 minutes incubation with peroxidase-labelled streptavidin. Plates were developed for 20 min using TMB as a substrate and the reaction was stopped by adding 0.5 M $H_2SO_4$. Optical density was measured as described above. Washing buffer was used for washing the plates between incubation steps (five times). Incubation steps were performed without shaking at room temperature. The assay positivity threshold set by the manufacturer was 200 mIU/ml.

## 2. <u>Data exclusion and data handling before statistical analysis</u>

The baseline sample collected from individuals who have had a natural infection more than 14 days before the administration of the first vaccine dose was excluded from the analyses. The days from baseline to the vaccine in infection-naïve individuals with a baseline sample collected before the administration of the first dose was reset to 0. Individuals vaccinated with a different vaccine to BNT162b2 were excluded from the analyses (n=124). Regarding statistical analyses to evaluate associations with SARS-CoV-2 reinfection, individuals who had a first infection with the virus after the administration of two doses of the BNT162b2 vaccine were excluded due to the lack of homogeneity in the antibody dynamics before the waning period after the administration of the second dose. A total of 14 individuals were excluded due to the uncertainty to identify whether the individual was infected with a variant earlier to Omicron or with Omicron. Individuals who did not receive the third dose were excluded from the study (n=4). R packages used in this study were

readxl (version 1.4.1), dplyr (version 1.0.9), tidyr (version 1.2.0), lubridate (version 1.8.0), writexl (version 1.4.0), glmmTMB (version 1.1.4), DHARMa (version 0.4.5), lmerTest (version 3.1.3), car (version 3.1.0), carData (version 3.0.5), lme4 (version 1.1.30), Matrix (version 1.3.3), ggplot2 (version 3.3.6), reshape (version 0.8.9), ggpubr (version 0.4.0), wesanderson (version 0.3.6), ggthemes (version 4.2.4), and ggnewscale (version 0.4.7).

## 3. Antibody response modeling

Antibody levels and responses over time were evaluated using generalized mixed models with and without cubic splines included in the R package glmmTMB[3]. The R package DHARMa (https://cran.r-project.org/web/packages/DHARMa/index.html) was employed for all the mixed models to check the model fitness and to evaluate diagnostics of the residuals. The models used in this study were described in a previous publication by our group[4] and modified accordingly to fit the new study cohort.

### 3.1. Two-part independent modeling of antibody waning and peak projection after boost

Due to the study design, there was insufficient observed data between the 6-month and 12-month round to evaluate the antibody decline until boost administration and the peak generated after this event. To evaluate this, we fitted a two-part independent model, the first part consisted of the modelling of the prime dynamics and the second part modelling of the boost dynamics.

#### 3.1.1. IgG and neutralizing antibody (nAb) levels – Independent model

##### 3.1.1.1. First part of the independent model

Log10-transformed IgG/nAbs levels were fitted in the zero-inflated Gaussian mixed model with subject-level random effects for both intercept and slope across days from first vaccination dose. Days from first vaccination dose were represented with two natural cubic splines (NCS), allowing the modeling of non-linear trends. The knots of the two NCS were defined based on median of the days from first vaccination at 21-day and the peak reached after 2-month sample collection times. Alongside the two NCS, infection status, age groups and sex were fitted in the model. Moreover, a two-way interaction between NCS and infection status, NCS and age groups, and between infection status and age groups (only for IgG) were included to evaluate IgG/nAbs dynamics over time. Days from first vaccination dose, infection status, and sex were included as

independent variables for the zero-inflated model. This model was used to project the IgG/nAbs levels until day 295 from the first vaccine dose (median days of boost administration).

#### 3.1.1.2. Second part of the independent model

Log10-transformed IgG/nAbs levels were fitted in the linear mixed model with subject-level random effect for both intercept and slope across days from the first vaccination dose. Variables included in the linear mixed model were days from first vaccination dose, infection status, age groups, and sex. Moreover, a two-way interaction between days from the first vaccine and infection status, days from the first dose and age groups, and between infection status and age groups (only for IgG) were included to evaluate the IgG/nAbs dynamics over time. This model was used to project the IgG/nAbs levels from day 309 from the first vaccine dose.

Predicted data from the first and the second part of the independent models were merged and used to plot the IgG/nAbs dynamics over time.

### 3.1.2. IgA responses – Independent model

#### 3.1.2.1. First part of the independent model

Binary responses of positive IgA responses were fitted using a GLMM with binomial distribution and with subject-level random effects for intercept. Days from first vaccination dose were represented with two NCS, allowing the modeling of non-linear trends. The knots of the two NCS were defined based on median of the days from first vaccination at 21-day and the peak reached after 2-month sample collection times. Alongside the two NCS, infection status, age groups, and sex were fitted in the model. Moreover, a two-way interaction between NCS and infection status was included to evaluate the IgA responses over time. This model was used to predict the probability of positive IgA responses until day 295 from the first vaccine dose (median days of boost administration).

#### 3.1.2.2. Second part of the independent model

Binary responses of positive IgA responses were fitted in the GLMM with subject-level random effect for both intercept and slope across days from the first vaccination dose. Variables included in the GLMM were days from first vaccination dose, infection status, age groups, and sex. Moreover, a two-way interaction

between days from the first vaccine and infection status was included to evaluate the IgA responses dynamics over time. This model was used to project the probability of positive IgA responses from day 309 from the first vaccine dose.

Predicted data from the first and the second part of the independent models were merged and used to plot the IgA responses dynamics over time.

### 3.2. IgG levels

Zero-inflated Gaussian mixed models were employed to evaluate the levels of IgG as the baseline levels presented a high proportion of samples with non-detectable IgG. This correction was necessary to assume the normal distribution of the IgG levels data. Therefore, the zero-inflated Gaussian mixed model consisted of two parts, one based on a conditional model that fitted a Gaussian mixed model for the detectable IgG levels (also referred as non-zero observations), and another part that based on a zero-inflated model that fitted a binary model for the detectable vs non-detectable IgG levels (fitting the probability of observing a zero observation or not).

Log10-transformed IgG levels were fitted in the zero-inflated Gaussian mixed model with subject-level random effects for both intercept and slope across days from first vaccination dose. Days from first vaccination dose were represented with five NCS, allowing the modeling of non-linear trends. The knots of the five NCS were defined based on median of the days from first vaccination at 21-day, 2-month, 6-month, and 12-month sample collection times.

#### 3.2.1. IgG levels associated with infection status

Alongside the five NCS, infection status, age groups and sex were fitted in the model. Moreover, a two-way interaction between NCS and infection status, NCS and age groups, NCS and sex, infection status and age groups, and between infection status and sex were included to evaluate IgG dynamics over time. Days from first vaccination dose, infection status, and sex were included as independent variables for the zero-inflated model.

#### 3.2.2. IgG levels associated with reinfections

Alongside the five NCS, reinfection status, age groups and sex were fitted in the model. Moreover, a two-way interaction between NCS and reinfection status was included to evaluate IgG dynamics over time. Interactions between NCS and age groups, and NCS and sex were not included because of the lack of significance.

#### 3.2.3. IgG levels associated with future infections

Alongside the five NCS, future infection status, age groups, and sex were fitted in the model. Moreover, a two-way interaction between NCS and future infection status, NCS and age groups, and NCS and sex were included to evaluate IgG dynamics over time. Days from first vaccination dose was included as independent variable for the zero-inflated model.

#### 3.2.4. IgG antibody levels associated with immune imprinting

Alongside the five NCS, immune imprinting status, age groups, and sex were fitted in the model. Moreover, a two-way interaction between NCS and immune imprinting status, NCS and age groups, and NCS and sex were included to evaluate IgG dynamics over time. Days from first vaccination, immune imprinting status, and sex were included as independent variables for the zero-inflated model.

### 3.3. Neutralizing antibodies levels

Zero-inflated Gaussian mixed models were employed to evaluate the levels of neutralizing antibodies as the baseline levels presented a high proportion of samples with non-detectable neutralizing antibodies. This correction was necessary to assume the normal distribution of the neutralizing antibodies levels data. The zero-inflated Gaussian mixed model consisted of two parts, one based on a conditional model that fitted a Gaussian mixed model for the detectable neutralizing antibodies levels (also referred as non-zero observations), and another part that was based on a zero-inflated model that fitted a binary model for the detectable vs non-detectable neutralizing antibodies levels (fitting the probability of observing a zero observation or not).

Log10-transformed neutralizing antibodies levels were fitted in the zero-inflated Gaussian mixed model with subject-level random effects for both intercept and slope across days from first vaccination dose. Days from first vaccination dose were represented with five natural cubic splines (NCS), allowing the modeling of non-

linear trends. The knots of the five NCS were defined based on median of the days from first vaccination at 21-day, 2-month, 6-month, and 12-month sample collection times.

### 3.3.1. Neutralizing antibodies levels associated with infection status

Alongside the five NCS, infection status, age groups and sex were fitted in the model. Moreover, a two-way interaction between NCS and infection status, NCS and age groups, and NCS and sex were included to evaluate neutralizing antibodies dynamics over time. Interaction between infection status and age groups, and infection status and sex were not included because of the lack of significance. Days from first vaccination dose was included as independent variable for the zero-inflated model.

### 3.3.2. Neutralizing antibodies levels associated with reinfections

For this analysis, the zero-inflated model was not included as the proportion of non-detectable neutralizing antibodies was low in this subgroup.

Alongside the five NCS, reinfection status, age groups, and sex were fitted in the model. Moreover, a two-way interaction between NCS and reinfection status was included to evaluate neutralizing antibodies dynamics over time. Interaction between NCS and age groups or sex were not included because of the lack of significance.

### 3.3.3. Neutralizing antibodies levels associated with future infections

Alongside the five NCS, future infection status, age groups, and sex were fitted in the model. Moreover, a two-way interaction between NCS and future infection status, NCS and age groups, and NCS and sex were included to evaluate IgG dynamics over time.

### 3.3.4. Neutralizing antibodies levels associated with immune imprinting

Alongside the five NCS, immune imprinting status, age groups and sex were fitted in the model. Moreover, a two-way interaction between NCS and immune imprinting status was included to evaluate neutralizing antibodies dynamics over time. Interaction between NCS and age groups, and NCS and sex were not included due to the sample size.

### 3.4. IgA responses: Binomial generalized mixed model

Binomial generalized mixed models were used to model IgA responses over time after first vaccination dose. Binary responses of positive IgA responses with subject-level random effects for intercept were fitted. Days from first vaccination dose were represented with five NCS, allowing the modeling of non-linear trends. The knots of the five NCS were defined based on median of the days from first vaccination at 21-day, 2-month, 6-month, and 12-month sample collection times.

#### 3.4.1. IgA responses associated with infection status

Alongside the five NCS, infection status, age groups, and sex were fitted in the model. Moreover, a two-way interaction between NCS and infection status, and NCS and age groups were included to evaluate the IgA responses over time. Interaction between NCS and sex was not included because of the lack of significance.

#### 3.4.2. IgA responses associated with reinfection

Alongside the five NCS, reinfection status, age groups, and sex were fitted in the model. Moreover, a two-way interaction between NCS and reinfection status, and NCS and age groups were included to evaluate the IgA responses over time. Interaction between NCS and sex was not included because of the lack of significance.

#### 3.4.3. IgA responses associated with future infection

Alongside the five NCS, future infection status, age groups, and sex were fitted in the model. Moreover, a two-way interaction between NCS and future infection status was included to evaluate the IgA responses over time. Interactions between NCS and age groups, and NCS and sex were not included because of the lack of significance.

#### 3.4.4. IgA responses associated with immune imprinting

Alongside the five NCS, future immune imprinting status, age groups, and sex were fitted in the model. Moreover, a two-way interaction between NCS and immune imprinting status was included to evaluate the IgA responses over time. Interactions between NCS and age groups, and NCS and sex were not included because of the lack of significance.

### 3.5. IFN-γ levels

Linear mixed models were employed to model IFN-γ levels over time from after first vaccination. Log10-transformed IFN-γ levels were fitted in the linear mixed model with subject-level random effects for both intercept and slope across days from first vaccination.

A zero-inflated linear mixed model was employed to evaluate levels of IFN-γ associated with infection status as the baseline levels presented a high proportion of samples with non-detectable IFN-γ levels. This correction was necessary to assume the normal distribution of the IFN-γ levels data. The zero-inflated Gaussian mixed model consisted of two parts, one based on a conditional model that fits a Gaussian mixed model for the detectable IFN-γ levels (also referred as non-zero observations), and another part that was based on a zero-inflated model that fits a binary model for the detectable vs non-detectable IFN-γ levels (fitting the probability of observing a zero or not).

#### 3.5.1. IFN-γ levels associated with infection status

Variables included in the linear mixed model were days from first vaccination dose, infection status, age groups, and sex. Moreover, a two-way interaction between days from the first vaccine and infection status was included to evaluate the IFN-γ dynamics over time. Infection status was included as independent variable for the zero-inflated model.

#### 3.5.2. IFN-γ levels associated with reinfection

The zero-inflated part was not included in this analysis as the proportion of non-detectable IFN-γ levels (also referred as zero observations) was low.

Variables included in the linear mixed model were days from first vaccination dose, reinfection status, age groups, and sex. Moreover, a two-way interaction between days from the first vaccine and reinfection status was included to evaluate the IFN-γ dynamics over time.

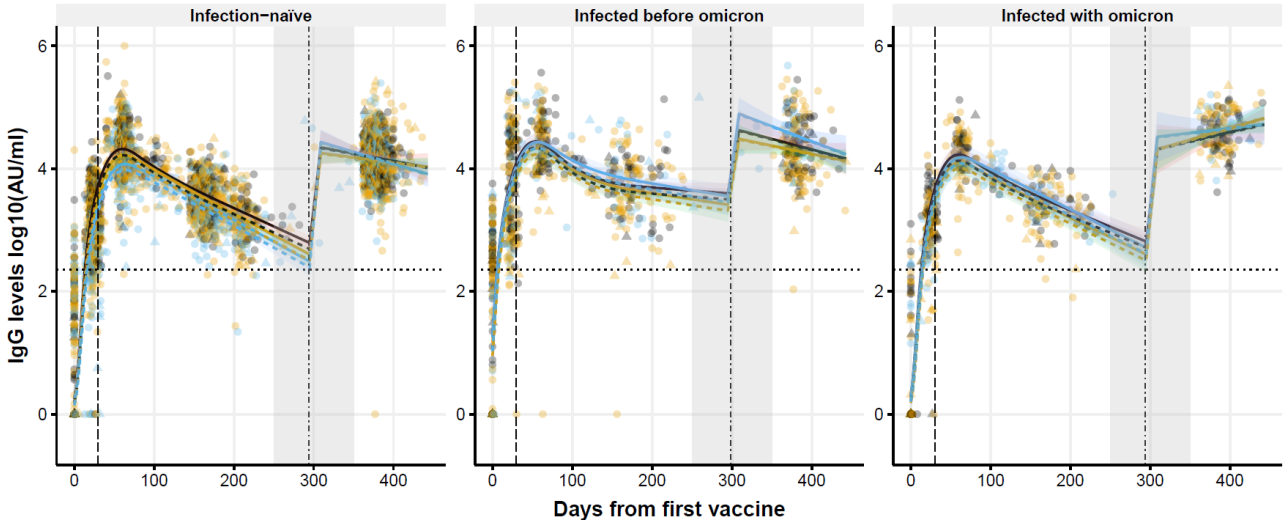
#### 3.5.3. IFN-γ levels associated with future infection

Variables included in the linear mixed model were days from first vaccination dose, future infection status, age groups, and sex. Moreover, a two-way interaction between days from the first vaccine and future infection status was included to evaluate the IFN-γ dynamics over time.

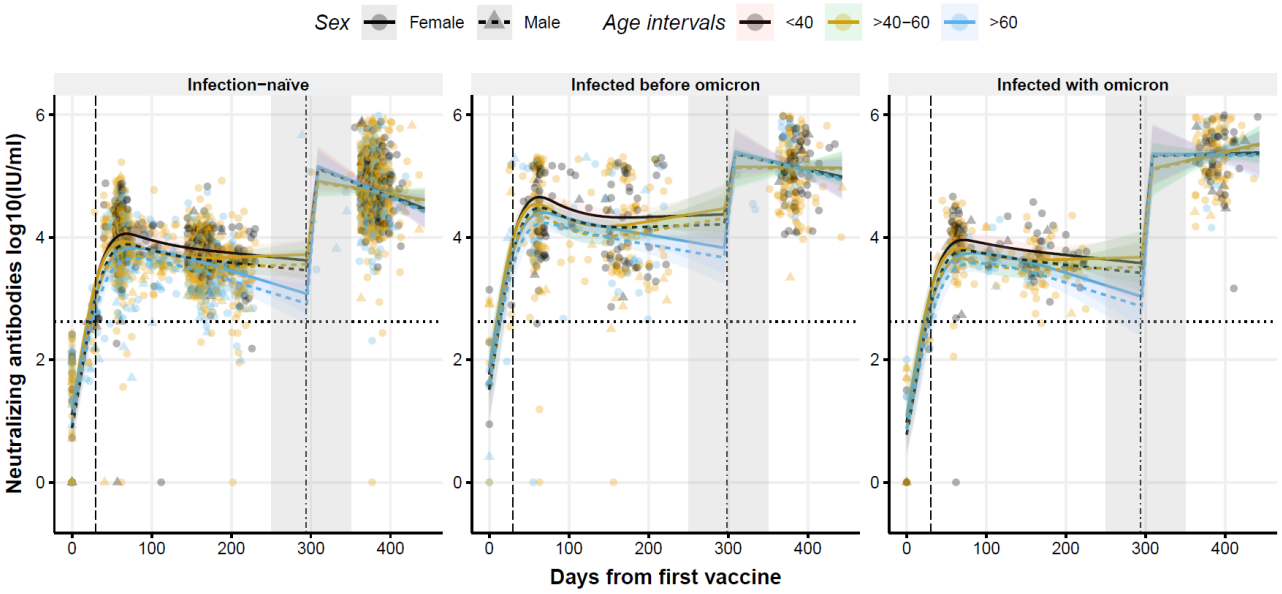
### 3.5.4. IFN-γ levels associated with immune imprinting

Variables included in the linear mixed model were days from first vaccination, immune imprinting status, age groups, and sex. Moreover, a two-way interaction between days from the first vaccine and immune imprinting status was included to evaluate the IFN-γ dynamics over time.

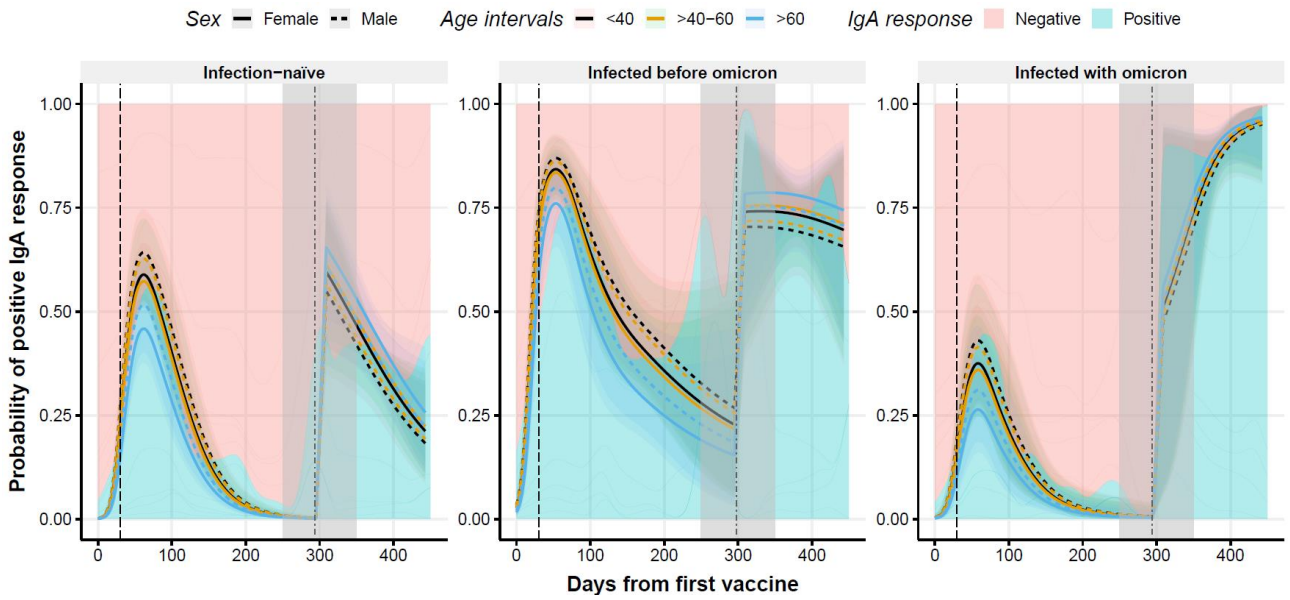
## Supplementary Figures



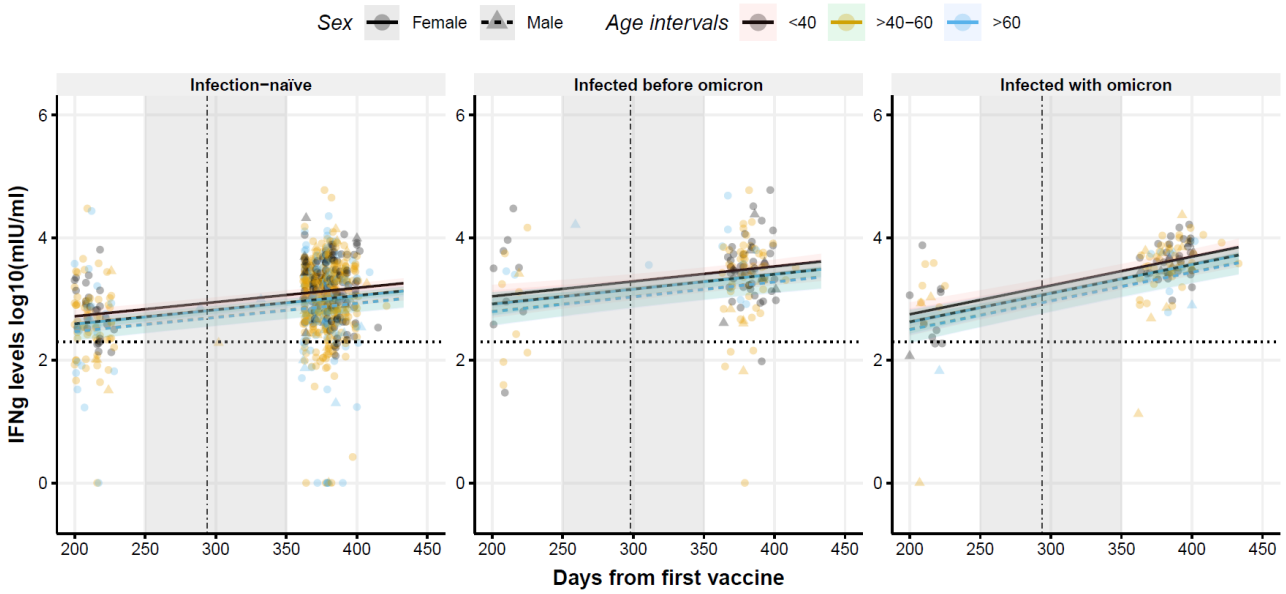

**Supplementary Figure 1. Dynamics of circulating IgG levels against RBD after the first dose of the BNT162b2 vaccine using two-part independent models.** Distribution of IgG levels, represented in log10(AU/ml), over time (days from the first vaccine) in infection-naïve individuals (left), in individuals previously infected with a variant before Omicron (middle), and in individuals infected with Omicron (right). Circles and triangles represent the observed levels of circulating IgG levels in females and males, respectively. Solid and dashed lines represent the predicted levels of circulating IgG levels calculated by the model in females and males, respectively. Black, yellow, and blue colors represent individuals with age <40, 40–60, and >60 years, respectively. Horizontal black dotted line represents the threshold for assay positivity. Vertical dashed and dashed-dotted lines represent when the second and the third dose was administered, respectively (median days). Shadowed areas represent the 95% confidence interval. Centre for the confidence interval is the predicted (mean) values. Predictive values in the grey-shaded area (days 250–350) do not represent a realistic projection due to insufficient observed data to provide realistic predictive data. Source data are provided as a Source Data file.



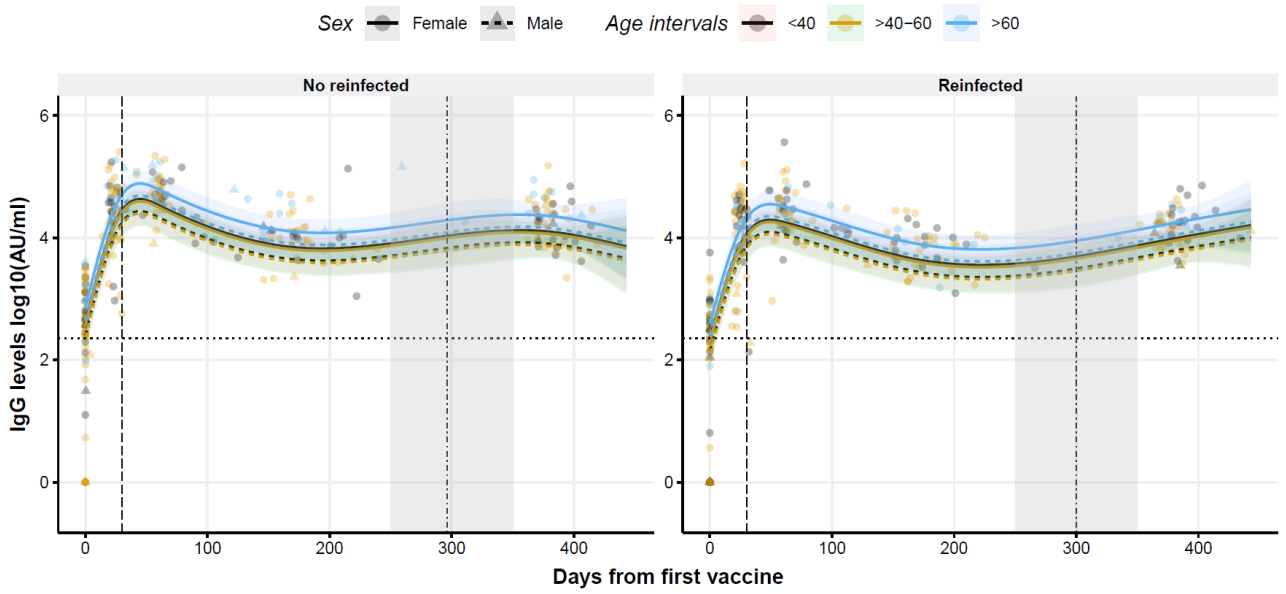

**Supplementary Figure 2. Dynamics of circulating neutralizing antibody levels against RBD after the first dose of the BNT162b2 vaccine using two-part independent models.** Distribution of neutralizing antibody levels, represented in log10(IU/ml), over time (days from the first vaccine) in infection-naïve individuals (left), in individuals previously infected with a variant before Omicron (middle), and in individuals infected with Omicron (right). Circles and triangles represent the observed levels of circulating neutralizing antibody in females and males, respectively. Solid and dashed lines represent the predicted levels of circulating neutralizing antibody calculated by the model in females and males, respectively. Black, yellow, and blue colors represent individuals with age <40, 40–60, and >60 years, respectively. Horizontal black dotted line represents the threshold for assay positivity. Vertical dashed and dashed-dotted lines represent when the second and the third dose was administered, respectively (median days). Shadowed areas represent the 95% confidence interval. Centre for the confidence interval is the predicted (mean) values. Predictive values in the grey-shaded area (days 250–350) do not represent a realistic projection due to insufficient observed data to provide realistic predictive data. Source data are provided as a Source Data file.



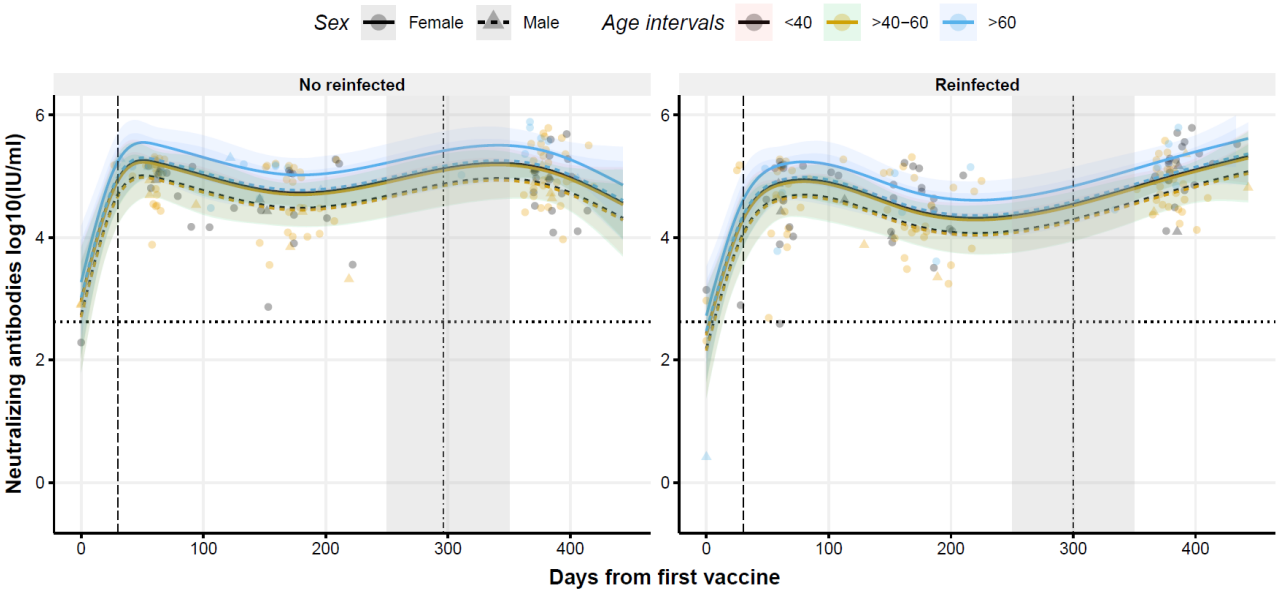

**Supplementary Figure 3. Observed and predicted probability of positive IgA responses against RBD after the first dose of the BNT162b2 vaccine using two-part independent models.** Distribution of positive IgA response (probability) over time (days from the first vaccine) in infection-naïve individuals (left), in individuals previously infected with a variant before Omicron (middle), and in individuals infected with Omicron (right). Blue and pink backgrounds represent the conditional density estimation of positive and negative IgA responses, respectively. Solid and dashed lines represent the predicted probability of positive IgA responses calculated by the model in females and males, respectively. Black, yellow, and blue colors represent individuals with age <40, 40–60, and >60 years, respectively. Vertical dashed and dashed-dotted lines represent when the second and the third dose was administered, respectively (median days). Shadowed areas represent the 95% confidence interval. Centre for the confidence interval is the predicted (mean) values. Predictive values in the grey-shaded area (days 250–350) do not represent a realistic projection due to insufficient observed data to provide realistic predictive data. Source data are provided as a Source Data file.



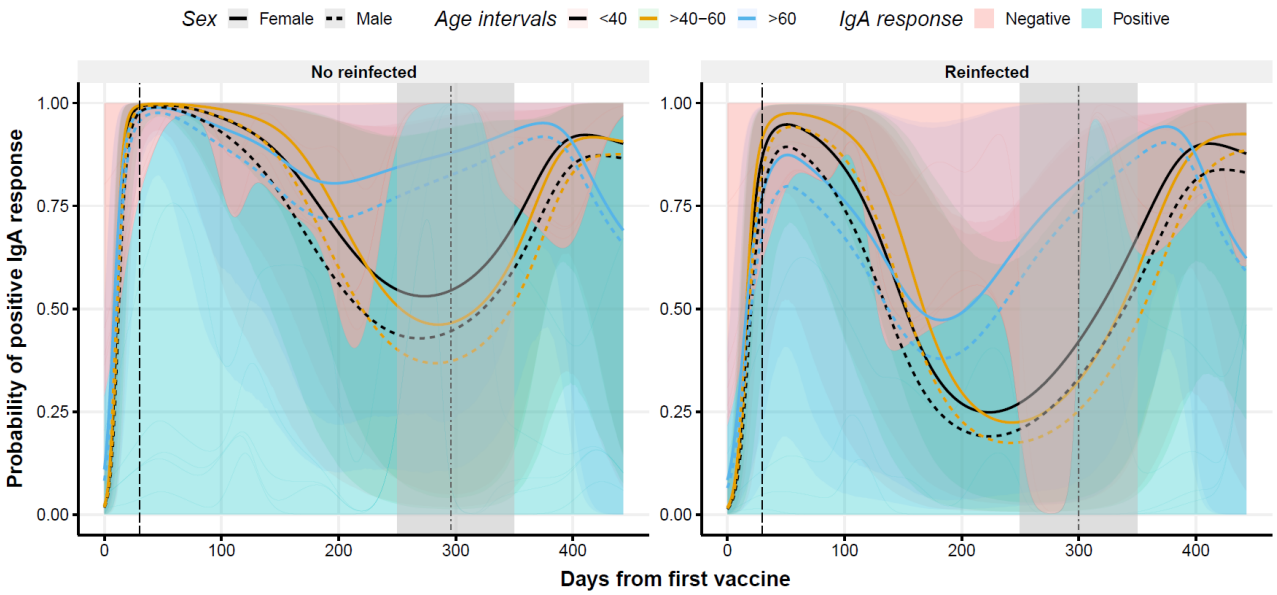

**Supplementary Figure 4. Dynamics of IFN-γ levels released after the first dose of the BNT162b2 vaccine using a linear model.** Distribution of IFN-γ levels, represented in log10(mIU/ml), over time (days from the first vaccine) in infection-naïve individuals (left), individuals infected with a variant before omicron (middle), and in individuals infected with Omicron (right). Circles and triangles represent the observed levels of IFN-γ levels released in females and males, respectively. Solid and dashed lines represent the predicted levels of IFN-γ levels released calculated by the model in females and males, respectively. Black, yellow, and blue colors represent individuals with age <40, 40–60, and >60 years, respectively. Horizontal black dotted line represents the threshold for assay positivity. Vertical dashed-dotted line represents when the third dose was administered (median days). Shadowed areas represent the 95% confidence interval. Centre for the confidence interval is the predicted (mean) values. Predictive values in the grey-shaded area (days 250–350) do not represent a realistic projection due to insufficient observed data to provide realistic predictive data. Source data are provided as a Source Data file.



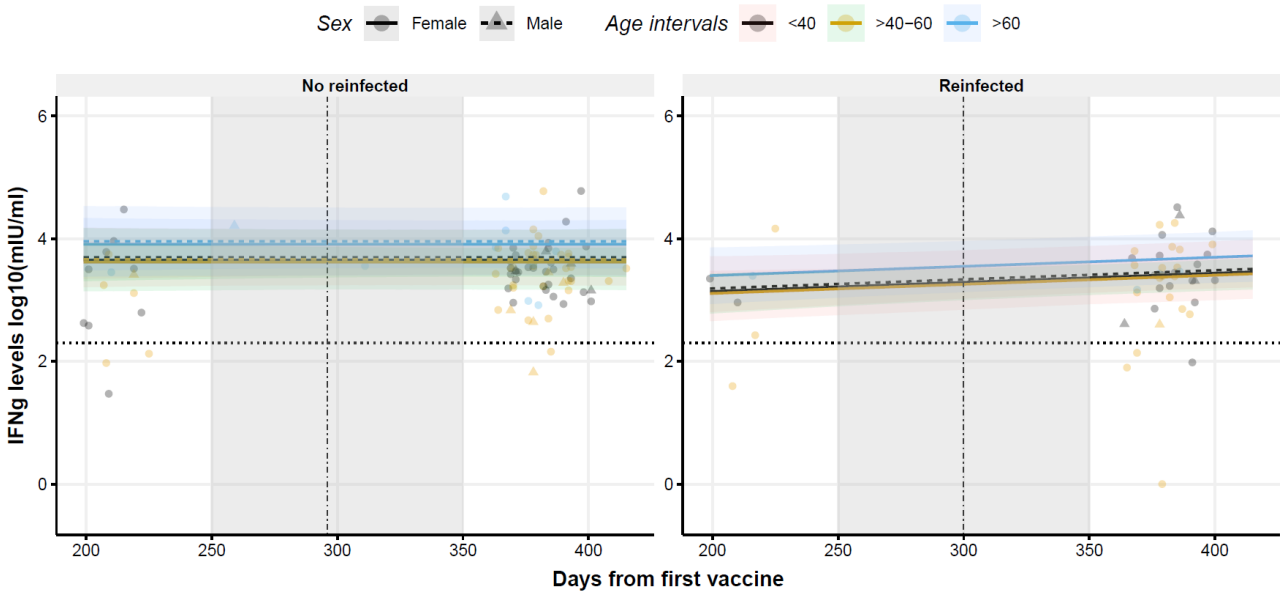

**Supplementary Figure 5. Dynamics of circulating IgG levels against RBD after the first dose of the BNT162b2 vaccine in naturally infected individuals before Omicron in relation to reinfection using a non-linear model.** Distribution of IgG levels, represented in log10(AU/ml), over time (days from the first vaccine) in individuals previously infected with a variant before Omicron without subsequent reinfection (left), and those who got a subsequent reinfection (right). Circles and triangles represent the observed levels of circulating IgG levels in females and males, respectively. Solid and dashed lines represent the predicted levels of circulating IgG levels calculated by the model in females and males, respectively. Black, yellow, and blue colors represent individuals with age <40, 40–60, and >60 years, respectively. Horizontal black dotted line represents the threshold for assay positivity. Vertical dashed and dashed-dotted lines represent when the second and the third dose was administered, respectively (median days). Shadowed areas represent the 95% confidence interval. Centre for the confidence interval is the predicted (mean) values. Predictive values in the grey-shaded area (days 250–350) do not represent a realistic projection due to insufficient observed data to provide realistic predictive data. Source data are provided as a Source Data file.



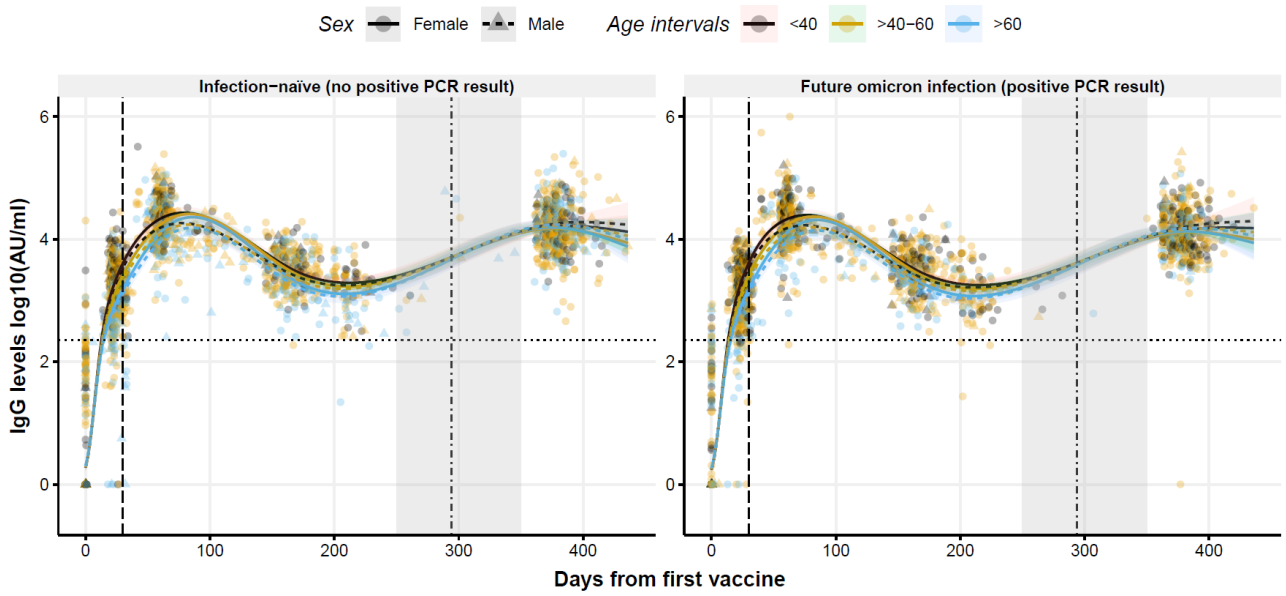

**Supplementary Figure 6. Dynamics of circulating neutralizing antibody levels against RBD after the first dose of the BNT162b2 vaccine in naturally infected individuals before Omicron in relation to reinfection using a non-linear model.** Distribution of neutralizing antibodies levels, represented in log10(IU/ml), over time (days from the first vaccine) in individuals previously infected with a variant before Omicron without subsequent reinfection (left), and those who got a subsequent reinfection (right). Circles and triangles represent the observed levels of circulating neutralizing antibodies in females and males, respectively. Solid and dashed lines represent the predicted levels of circulating neutralizing antibodies calculated by the model in females and males, respectively. Black, yellow, and blue colors represent individuals with age <40, 40–60, and >60 years, respectively. Horizontal black dotted line represents the threshold for assay positivity. Vertical dashed and dashed-dotted lines represent when the second and the third dose was administered, respectively (median days). Shadowed areas represent the 95% confidence interval. Centre for the confidence interval is the predicted (mean) values. Predictive values in the grey-shaded area (days 250–350) do not represent a realistic projection due to insufficient observed data to provide realistic predictive data. Source data are provided as a Source Data file.



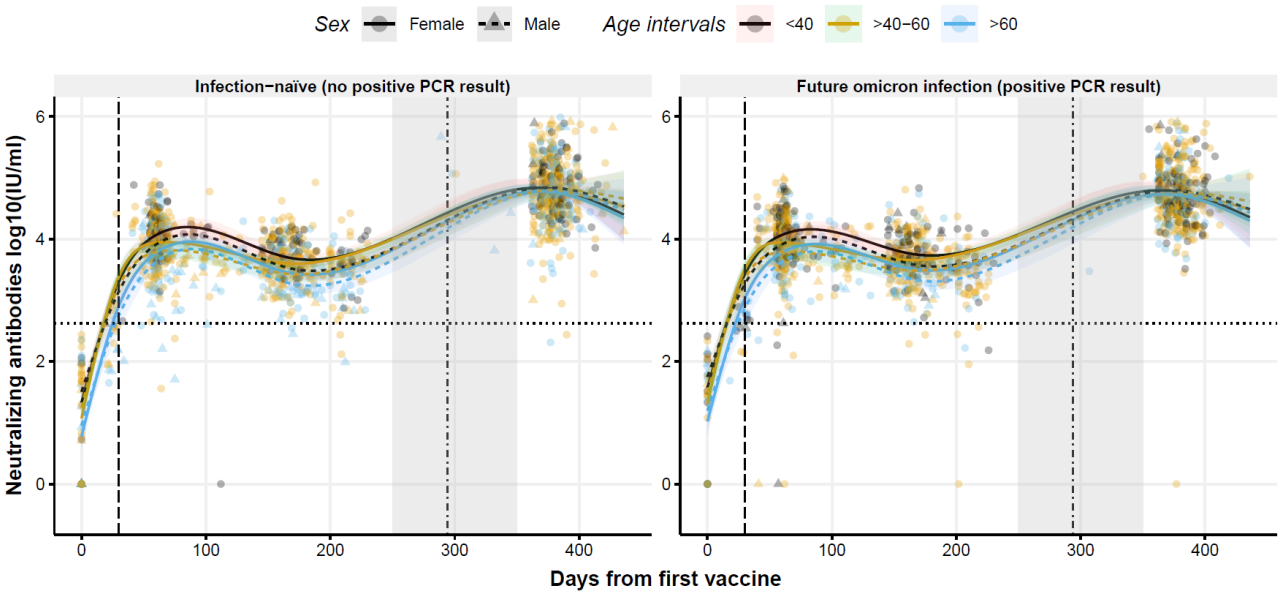

**Supplementary Figure 7. Observed and predicted probability of positive IgA responses against RBD after the first dose of the BNT162b2 vaccine naturally infected individuals before Omicron in relation to reinfection using a non-linear model.** Distribution of positive IgA response (probability) over time (days from the first vaccine) in individuals previously infected with a variant before Omicron without subsequent reinfection (left), and those who got a subsequent reinfection (right). Blue and pink backgrounds represent the conditional density estimation of positive and negative IgA responses, respectively. Solid and dashed lines represent the predicted probability of positive IgA responses calculated by the model in females and males, respectively. Vertical dashed and dashed-dotted lines represent when the second and the third dose was administered, respectively (median days). Shadowed areas represent the 95% confidence interval. Centre for the confidence interval is the predicted (mean) values. Predictive values in the grey-shaded area (days 250–350) do not represent a realistic projection due to insufficient observed data to provide realistic predictive data. Source data are provided as a Source Data file.



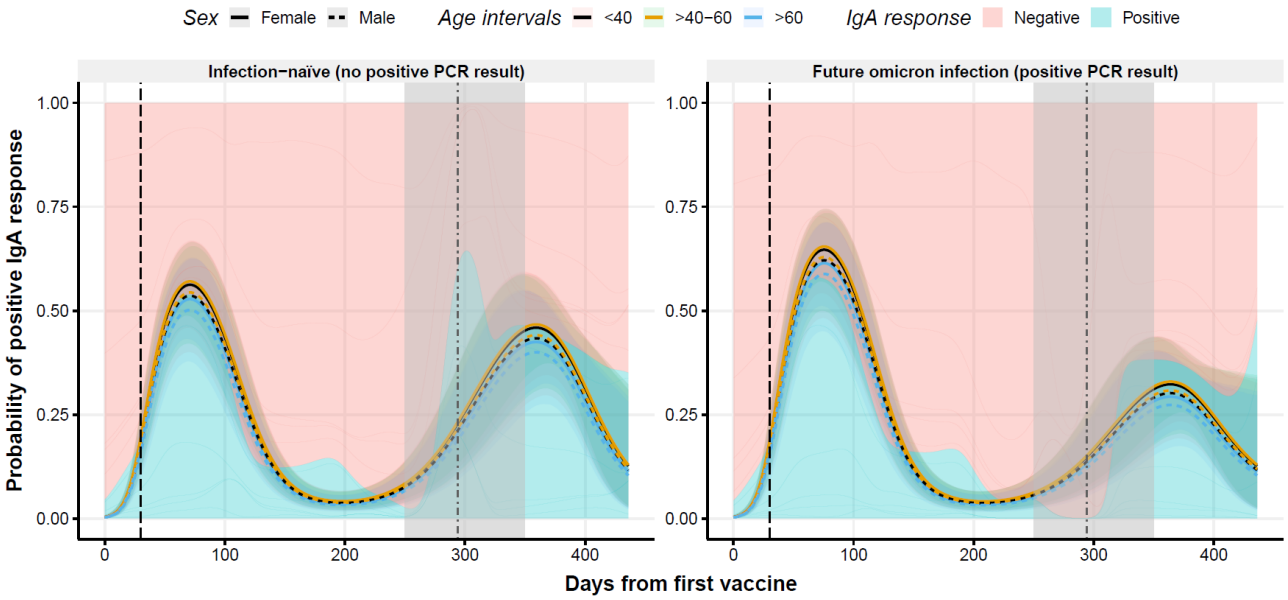

**Supplementary Figure 8. Dynamics of circulating IFN-γ levels released after the first dose of the BNT162b2 vaccine in naturally infected individuals before Omicron in relation to reinfection using a linear model.** Distribution of IFN-γ levels, represented in log10(AU/ml), over time (days from the first vaccine) in individuals previously infected with a variant before Omicron without subsequent reinfection (left), and those who got a subsequent reinfection (right). Circles and triangles represent the observed levels of IFN-γ levels released in females and males, respectively. Solid and dashed lines represent the predicted levels of IFN-γ levels released calculated by the model in females and males, respectively. Black, yellow, and blue colors represent individuals with age <40, 40–60, and >60 years, respectively. Horizontal black dotted line represents the threshold for assay positivity. Vertical dashed-dotted line represents when the third dose was administered (median days). Shadowed areas represent the 95% confidence interval. Centre for the confidence interval is the predicted (mean) values. Predictive values in the grey-shaded area (days 250–350) do not represent a realistic projection due to insufficient observed data to provide realistic predictive data. Source data are provided as a Source Data file.



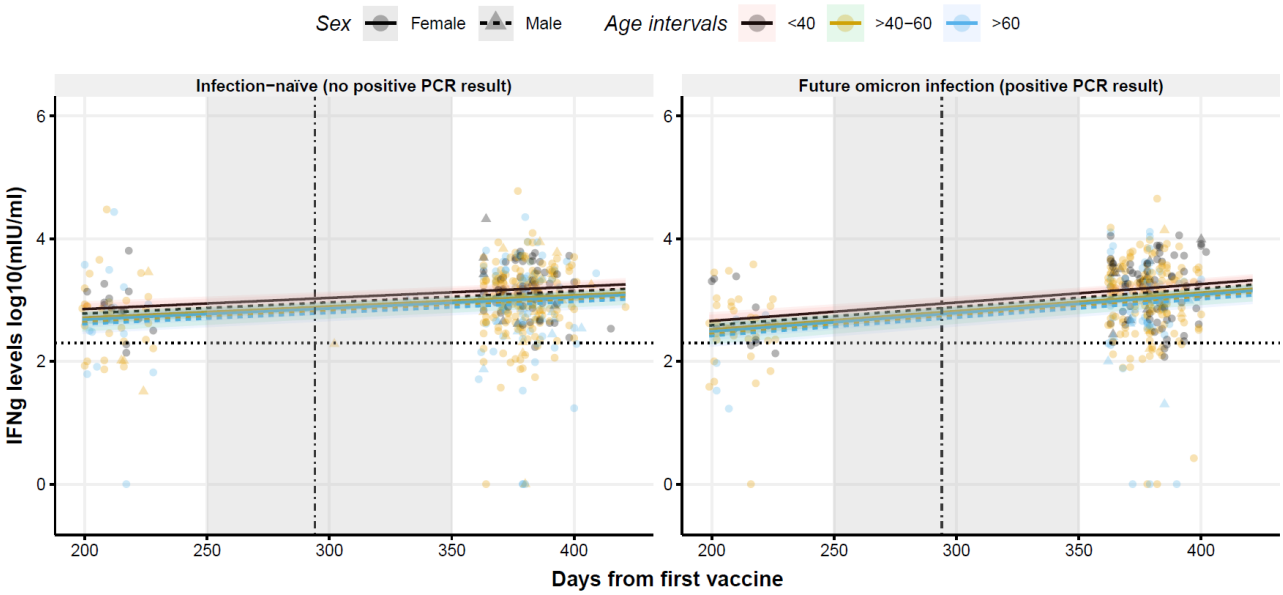

**Supplementary Figure 9. Dynamics of circulating IgG levels against RBD after the first dose of the BNT162b2 vaccine in infection-naïve individuals in relation to future infection using a non-linear model.** Distribution of IgG levels, represented in log10(AU/ml), over time (days from the first vaccine) in infection-naïve individuals who do not get a future infection (left), and those who get a future infection with Omicron (right). Circles and triangles represent the observed levels of circulating IgG levels in females and males, respectively. Solid and dashed lines represent the predicted levels of circulating IgG levels calculated by the model in females and males, respectively. Black, yellow, and blue colors represent individuals with age <40, 40–60, and >60 years, respectively. Horizontal black dotted line represents the threshold for assay positivity. Vertical dashed and dashed-dotted lines represent when the second and the third dose was administered, respectively (median days). Shadowed areas represent the 95% confidence interval. Centre for the confidence interval is the predicted (mean) values. Predictive values in the grey-shaded area (days 250–350) do not represent a realistic projection due to insufficient observed data to provide realistic predictive data. Source data are provided as a Source Data file.



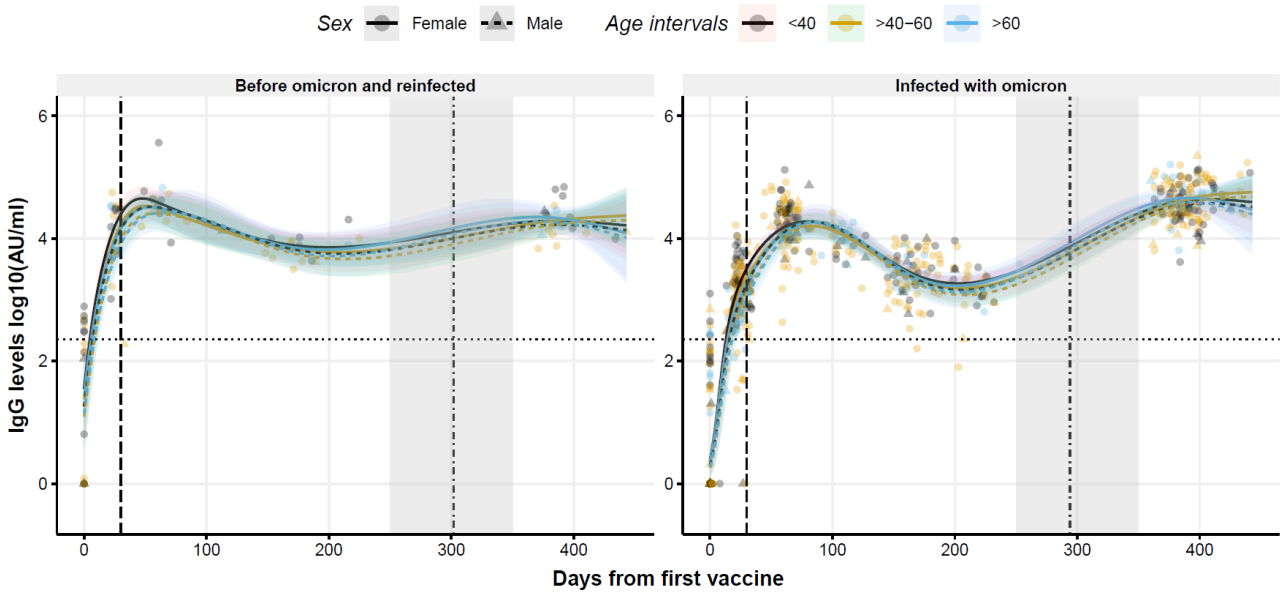

**Supplementary Figure 10. Dynamics of circulating neutralizing antibody levels against RBD after the first dose of the BNT162b2 vaccine in infection-naïve individuals in relation to future infection using a non-linear model.** Distribution of neutralizing antibodies levels, represented in log10(IU/ml), over time (days from the first vaccine) in infection-naïve individuals who do not get a future infection (left), and those who get a future infection with Omicron (right). Circles and triangles represent the observed levels of circulating neutralizing antibody levels in females and males, respectively. Solid and dashed lines represent the predicted levels of circulating neutralizing antibody levels calculated by the model in females and males, respectively. Black, yellow, and blue colors represent individuals with age <40, 40–60, and >60 years, respectively. Horizontal black dotted line represents the threshold for assay positivity. Vertical dashed and dashed-dotted lines represent when the second and the third dose was administered, respectively (median days). Shadowed areas represent the 95% confidence interval. Centre for the confidence interval is the predicted (mean) values. Predictive values in the grey-shaded area (days 250–350) do not represent a realistic projection due to insufficient observed data to provide realistic predictive data. Source data are provided as a Source Data file.



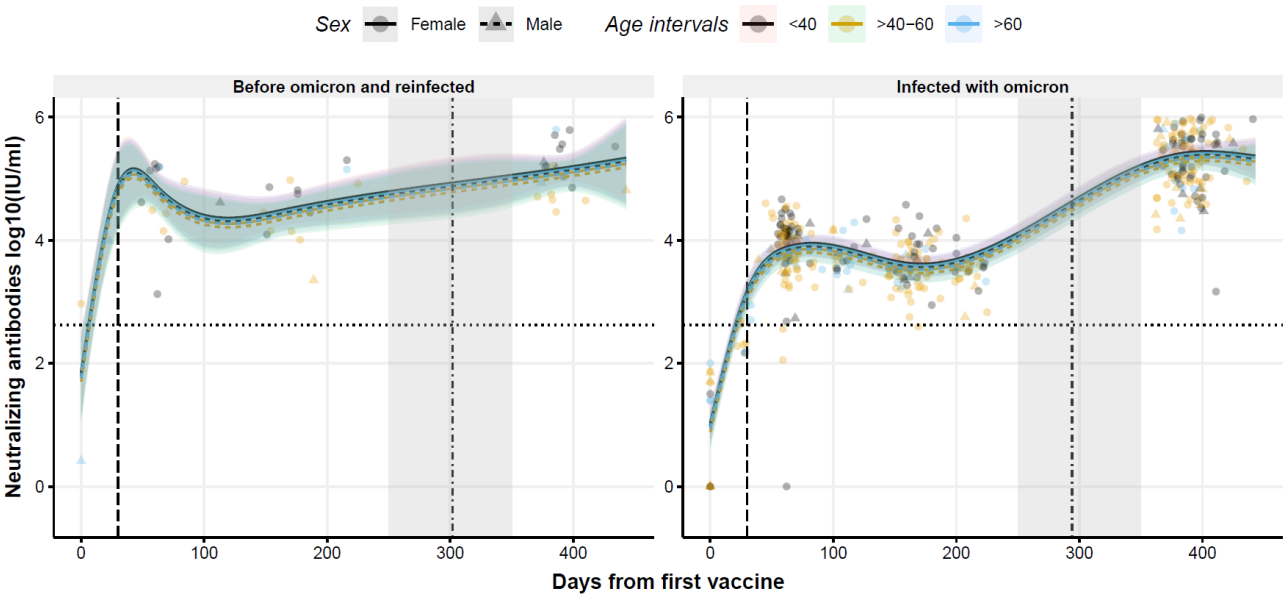

**Supplementary Figure 11. Observed and predicted probability of positive IgA responses against RBD after the first dose of the BNT162b2 vaccine in infection-naïve individuals in relation to future infection using a non-linear model.** Distribution of positive IgA response (probability) over time (days from the first vaccine) in infection-naïve individuals who do not get a future infection (left), and those who get a future infection with Omicron (right). Blue and pink backgrounds represent the conditional density estimation of positive and negative IgA responses, respectively. Solid and dashed lines represent the predicted probability of positive IgA responses calculated by the model in females and males, respectively. Black, yellow, and blue colors represent individuals with age <40, 40–60, and >60 years, respectively. Vertical dashed and dashed-dotted lines represent when the second and the third dose was administered, respectively (median days). Shadowed areas represent the 95% confidence interval. Centre for the confidence interval is the predicted (mean) values. Predictive values in the grey-shaded area (days 250–350) do not represent a realistic projection due to insufficient observed data to provide realistic predictive data. Source data are provided as a Source Data file.



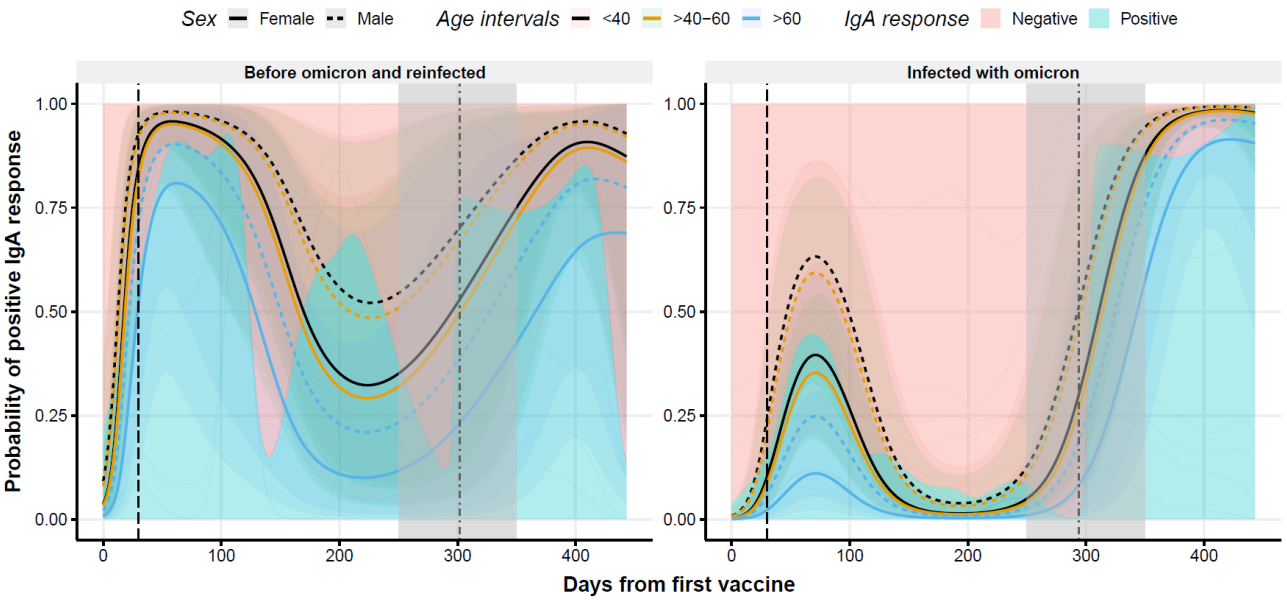

**Supplementary Figure 12. Dynamics of IFN-γ levels released after the first dose of the BNT162b2 vaccine in infection-naïve individuals in relation to future infection using a linear model.** Distribution of IFN-γ levels, represented in log10(mIU/ml), over time (days from the first vaccine) in infection-naïve individuals who do not get a future infection (left), and those who get a future infection with Omicron (right). Circles and triangles represent the observed levels of IFN-γ levels released in females and males, respectively. Solid and dashed lines represent the predicted levels of IFN-γ levels released calculated by the model in females and males, respectively. Black, yellow, and blue colors represent individuals with age <40, 40–60, and >60 years, respectively. Horizontal black dotted line represents the threshold for assay positivity. Vertical dashed-dotted line represents when the third dose was administered (median days). Shadowed areas represent the 95% confidence interval. Centre for the confidence interval is the predicted (mean) values. Predictive values in the grey-shaded area (days 250–350) do not represent a realistic projection due to insufficient observed data to provide realistic predictive data. Source data are provided as a Source Data file.



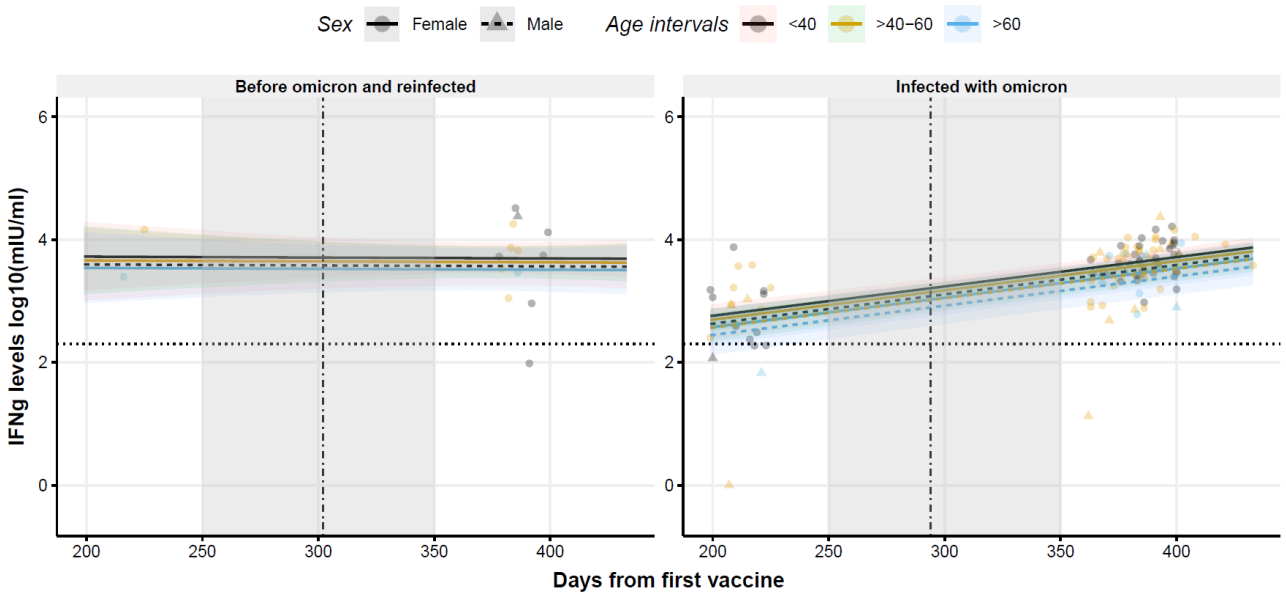

**Supplementary Figure 13. Dynamics of circulating IgG levels against RBD after the first dose of the BNT162b2 vaccine in infected individuals with different immune imprinting status using a non-linear model.** Distribution of IgG levels, represented in log10(AU/ml), over time (days from the first vaccine) in individuals previously infected before Omicron who got reinfected (left), and individuals infected with Omicron (right). Circles and triangles represent the observed levels of circulating IgG levels in females and males, respectively. Solid and dashed lines represent the predicted levels of circulating IgG levels calculated by the model in females and males, respectively. Black, yellow, and blue colors represent individuals with age <40, 40–60, and >60 years, respectively. Horizontal black dotted line represents the threshold for assay positivity. Vertical dashed and dashed-dotted lines represent when the second and the third dose was administered, respectively (median days). Shadowed areas represent the 95% confidence interval. Centre for the confidence interval is the predicted (mean) values. Predictive values in the grey-shaded area (days 250–350) do not represent a realistic projection due to insufficient observed data to provide realistic predictive data. Source data are provided as a Source Data file.




**Supplementary Figure 14. Dynamics of circulating neutralizing antibody levels against RBD after the first dose of the BNT162b2 vaccine in individuals with different immune imprinting status using a non-linear model.** Distribution of neutralizing antibody levels, represented in log10(IU/ml), over time (days from the first vaccine) in individuals previously infected before Omicron who got reinfected (left), and individuals infected with Omicron (right). Circles and triangles represent the observed levels of circulating neutralizing antibody levels in females and males, respectively. Solid and dashed lines represent the predicted levels of circulating neutralizing antibody levels calculated by the model in females and males, respectively. Black, yellow, and blue colors represent individuals with age <40, 40–60, and >60 years, respectively. Horizontal black dotted line represents the threshold for assay positivity. Vertical dashed and dashed-dotted lines represent when the second and the third dose was administered, respectively (median days). Shadowed areas represent the 95% confidence interval. Centre for the confidence interval is the predicted (mean) values. Predictive values in the grey-shaded area (days 250–350) do not represent a realistic projection due to insufficient observed data to provide realistic predictive data. Source data are provided as a Source Data file.




**Supplementary Figure 15. Observed and predicted probability of positive IgA responses against RBD after the first dose of the BNT162b2 vaccine in individuals with different immune imprinting status using a non-linear model.** Distribution of IgA responses (probability), over time (days from the first vaccine) in individuals infected before Omicron who got reinfected (left), and individuals infected with Omicron (right). Blue and pink backgrounds represent the conditional density estimation of positive and negative IgA responses, respectively. Solid and dashed lines represent the predicted probability of positive IgA responses calculated by the model in females and males, respectively. Black, yellow, and blue colors represent individuals with age <40, 40–60, and >60 years, respectively. Vertical dashed and dashed-dotted lines represent when the second and the third dose was administered, respectively (median days). Shadowed areas represent the 95% confidence interval. Centre for the confidence interval is the predicted (mean) values. Predictive values in the grey-shaded area (days 250–350) do not represent a realistic projection due to insufficient observed data to provide realistic predictive data. Source data are provided as a Source Data file.




**Supplementary Figure 16. Dynamics of IFN-γ levels released after the first dose of the BNT162b2 vaccine in individuals infected with different immune imprinting status using a linear model.** Distribution of IFN-γ levels released, represented in log10(mIU/ml), over time (days from the first vaccine) in individuals infected before Omicron who got reinfected (left), and individuals infected with Omicron (right). Circles and triangles represent the observed levels of IFN-γ levels released in females and males, respectively. Solid and dashed lines represent the predicted levels of IFN-γ levels released calculated by the model in females and males, respectively. Black, yellow, and blue colors represent individuals with age <40, 40–60, and >60 years, respectively. Horizontal black dotted line represents the threshold for assay positivity. Vertical dashed-dotted line represents when the third dose was administered (median days). Shadowed areas represent the 95% confidence interval. Centre for the confidence interval is the predicted (mean) values. Predictive values in the grey-shaded area (days 250–350) do not represent a realistic projection due to insufficient observed data to provide realistic predictive data. Source data are provided as a Source Data file.

## Supplementary Tables

### Supplementary Table 1. Demographic data and characteristics of the subgroup study cohorts

| | Reinfection cohort (N=119) | | Future infection cohort (N=955) * | | Immune imprinting cohort (N=185) | |
|---|---|---|---|---|---|---|
| | Not reinfected (N=62) | Reinfected (N=57) | Not future infected (N=492) | Future infected (N=463) | Before omicron (N=22) | Omicron (N=163) |
| **Sex** | | | | | | |
| Female | 53 (85.5%) | 51 (89.5%) | 419 (85.2%) | 414 (89.4%) | 18 (81.8%) | 132 (81.0%) |
| Male | 9 (14.5%) | 6 (10.5%) | 73 (14.8%) | 49 (10.6%) | 4 (18.2%) | 31 (19.0%) |
| **Age (years)** | | | | | | |
| Median (IQR) | 48 (33–55) | 45 (35–56) | 55 (46–61) | 51 (41–59) | 42 (35–49) | 46 (39–55) |
| <40 | 19 (30.6%) | 21 (36.8%) | 81 (16.5%) | 112 (24.2%) | 11 (50.0%) | 53 (32.5%) |
| >40–60 | 35 (56.5%) | 30 (52.6%) | 267 (54.3%) | 251 (54.2%) | 8 (36.4%) | 93 (57.1%) |
| >60 | 8 (12.9%) | 6 (10.5%) | 144 (29.3%) | 100 (21.6%) | 3 (13.6%) | 17 (10.4%) |
| **BMI** | | | | | | |
| Median (IQR) | 25 (22–29) [a] | 24 (22–25) [b] | 24 (22–28) [c] | 24 (22–27) [d] | 23 (21–25) [e] | 24 (22–26) [f] |
| Underweight | 0 (0%) | 2 (3.8%) | 8 (1.8%) | 2 (0.5%) | 0 (0%) | 1 (0.8%) |
| Normal | 30 (49.2%) | 36 (67.9%) | 235 (53.9%) | 245 (58.8%) | 13 (72.2%) | 86 (64.7%) |
| Overweight | 20 (32.8%) | 11 (20.8%) | 122 (28.0%) | 105 (25.2%) | 4 (22.2%) | 35 (26.3%) |
| Obese | 11 (18.0%) | 4 (7.5%) | 71 (16.3%) | 65 (15.6%) | 1 (5.6%) | 11 (8.3%) |
| **Time between first and second dose (days)** | | | | | | |
| Median (IQR) | 30 (28–33) | 30 (29–33) | 30 (29–32) | 30 (29–33) | 30 (28–33) | 30 (29–33) |
| **Time between first and third dose (days)** | | | | | | |
| Median (IQR) | 296 (287–302) | 300 (294–310) | 294 (286–302) | 294 (287–301) | 302 (296–325) | 294 (285–302) |
| **Time between second dose and Omicron infection (days)** | | | | | | |
| Median (IQR) | N.A. | N.A. | N.A. | N.A. | 338 (324–348) [g] | 337 (324–348) [g] |

| | Reinfection cohort (N=119) | | Future infection cohort (N=955) * | | Immune imprinting cohort (N=185) | |
|---|---|---|---|---|---|---|
| | **Not reinfected (N=62)** | **Reinfected (N=57)** | **Not future infected (N=492)** | **Future infected (N=463)** | **Before omicron (N=22)** | **Omicron (N=163)** |
| **Time between third dose and Omicron infection (days)** | | | | | | |
| Median (IQR) | N.A. | N.A. | N.A. | N.A. | 64 (49–80) [h] | 74 (64–84) [h] |
| **Time from sample to Omicron infection (days)** | | | | | | |
| Median (IQR) | N.A. | N.A. | N.A. | N.A. | 18 (10–24) [i] | 20 (14–27) [i] |

*Future infection based on a positive RT-PCR result after the 12-month sampling round

[a] Missing value: 1 individual. [b] Missing values: 4 individuals. [c] Missing values: 56 individuals. [d] Missing values: 46 individuals. [e] Missing values: 4 individuals. [f] Missing values: 30 individuals

[g] p=0.8138 (Mann-Whitney test, two-sided). [h] p=0.0889 (Mann-Whitney test, two-sided). [i] p=0.3331 (Mann-Whitney test, two-sided). $p<0.05$ was considered significant.

IQR: Interquartile range

N.A.: Not applicable

**Supplementary Table 2. Predicted mean IgG levels, represented in AU/ml, in individuals after the administration first vaccination dose according to infection status, age group, and sex**

| Days from 1st vaccine [a] | Infection status | Age Group | Sex | Geometric mean | CI 2.5% | CI 97.5% |
|---|---|---|---|---|---|---|
| 79 | Infection-naïve | <40 | Female | 26107.3 | 21798.5 | 31207.7 |
| 60 | Infected before omicron | <40 | Female | 28684.5 | 22942.8 | 35984.4 |
| 79 | Infected with omicron | <40 | Female | 19354.5 | 14565.6 | 25611.7 |
| 389 | Infection-naïve | <40 | Female | 14999.2 | 13163.1 | 17131.0 |
| 378 | Infected before omicron | <40 | Female | 23820.9 | 19433.3 | 29240.6 |
| 380* | Infected with omicron | <40 | Female | 38648.3 | 30394.3 | 48714.2 |
| 83 | Infection-naïve | >40-60 | Female | 23926.1 | 21211.8 | 27015.4 |
| 70 | Infected before omicron | >40-60 | Female | 23292.5 | 18863.1 | 28772.3 |
| 83 | Infected with omicron | >40-60 | Female | 18665.5 | 14587.3 | 23910.6 |
| 387 | Infection-naïve | >40-60 | Female | 14094.5 | 12961.0 | 15345.1 |
| 377 | Infected before omicron | >40-60 | Female | 21710.4 | 18343.2 | 25733.0 |
| 425 | Infected with omicron | >40-60 | Female | 46531.2 | 32647.9 | 66143.2 |
| 85 | Infection-naïve | >60 | Female | 20934.7 | 17619.5 | 24898.7 |
| 77 | Infected before omicron | >60 | Female | 33438.1 | 23645.3 | 47307.1 |
| 85 | Infected with omicron | >60 | Female | 18532.9 | 12273.9 | 28098.7 |
| 373 | Infection-naïve | >60 | Female | 14982.1 | 13302.1 | 16886.8 |
| 364 | Infected before omicron | >60 | Female | 41707.6 | 30682.8 | 57098.5 |
| 388 | Infected with omicron | >60 | Female | 46695.2 | 32277.5 | 67879.6 |
| 79 | Infection-naïve | <40 | Male | 21008.6 | 16022.0 | 27441.0 |
| 60 | Infected before omicron | <40 | Male | 15154.4 | 10455.7 | 21982.8 |
| 80 | Infected with omicron | <40 | Male | 13082.2 | 8826.4 | 19413.1 |
| 391 | Infection-naïve | <40 | Male | 16547.4 | 13413.2 | 20496.0 |
| 381 | Infected before omicron | <40 | Male | 17201.6 | 12312.3 | 23958.5 |
| 380* | Infected with omicron | <40 | Male | 35519.9 | 25033.8 | 49900.3 |
| 83 | Infection-naïve | >40-60 | Male | 19277.0 | 15183.0 | 24321.6 |
| 70 | Infected before omicron | >40-60 | Male | 12340.9 | 8461.4 | 18072.5 |
| 83 | Infected with omicron | >40-60 | Male | 12631.4 | 8768.1 | 18414.4 |
| 387 | Infection-naïve | >40-60 | Male | 15511.8 | 13124.7 | 18376.3 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 380 | Infected before omicron | >40-60 | Male | 15661.8 | 11361.6 | 21525.0 |
| 431 | Infected with omicron | >40-60 | Male | 44169.1 | 24248.5 | 80014.7 |
| | | | | | | |
| 85 | Infection-naïve | >60 | Male | 16877.4 | 13069.0 | 21830.3 |
| 77 | Infected before omicron | >60 | Male | 17752.7 | 11198.5 | 27798.5 |
| 86 | Infected with omicron | >60 | Male | 12549.5 | 7669.8 | 20211.5 |
| 374 | Infection-naïve | >60 | Male | 16299.5 | 13544.3 | 19570.3 |
| 367 | Infected before omicron | >60 | Male | 29720.6 | 20005.4 | 44112.5 |
| 390 | Infected with omicron | >60 | Male | 43221.5 | 27876.8 | 66880.0 |

[a] The day from 1st vaccine is selected based on when the peak after the second dose and the third dose was reached according to the infection status, age group, and sex
* IgG peak after the third dose did not plateau. Instead, the median days from the 12-months sampling round was selected.
CI: Confidence of interval
Source data are provided as a Source Data file

**Supplementary Table 3. Predicted mean neutralizing antibody levels, represented in IU/ml, in individuals after the administration first vaccination dose according to infection status, age group, and sex**

| Days from 1st vaccine [a] | Infection status | Age Group | Sex | Geometric mean | CI 2.5% | CI 97.5% |
|---|---|---|---|---|---|---|
| 89 | Infection-naïve | <40 | Female | 14323.4 | 11010.7 | 18601.3 |
| 75 | Infected before omicron | <40 | Female | 40540.9 | 31088.3 | 52708.3 |
| 91 | Infected with omicron | <40 | Female | 11596.5 | 8229.9 | 16402.0 |
| 366 | Infection-naïve | <40 | Female | 66250.7 | 53613.6 | 81675.6 |
| 386 | Infected before omicron | <40 | Female | 146510.9 | 119373.0 | 180276.2 |
| 389 | Infected with omicron | <40 | Female | 241503.0 | 193067.3 | 302896.8 |
| 80 | Infection-naïve | >40-60 | Female | 8570.5 | 7303.6 | 10038.6 |
| 53 | Infected before omicron | >40-60 | Female | 31407.6 | 24249.1 | 40645.2 |
| 84 | Infected with omicron | >40-60 | Female | 6833.5 | 5118.1 | 9127.3 |
| 380 | Infection-naïve | >40-60 | Female | 59410.0 | 53527.7 | 65841.5 |
| 380* | Infected before omicron | >40-60 | Female | 137566.1 | 114249.3 | 166039.4 |
| 380 | Infected with omicron | >40-60 | Female | 223309.6 | 177122.6 | 281124.0 |
| 91 | Infection-naïve | >60 | Female | 9220.4 | 7176.4 | 11792.7 |
| 81 | Infected before omicron | >60 | Female | 25377.3 | 18278.8 | 35454.7 |
| 92 | Infected with omicron | >60 | Female | 7483.7 | 5176.6 | 10771.0 |
| 365 | Infection-naïve | >60 | Female | 66785.4 | 54835.1 | 81428.7 |
| 378 | Infected before omicron | >60 | Female | 144622.0 | 115167.1 | 182531.2 |
| 384 | Infected with omicron | >60 | Female | 235739.8 | 180479.9 | 307463.4 |
| 84 | Infection-naïve | <40 | Male | 9508.3 | 6647.0 | 13653.2 |
| 64 | Infected before omicron | <40 | Male | 29014.6 | 21406.8 | 39330.1 |
| 87 | Infected with omicron | <40 | Male | 7638.5 | 4980.0 | 11715.2 |
| 363 | Infection-naïve | <40 | Male | 66500.5 | 48285.1 | 91530.6 |
| 377 | Infected before omicron | <40 | Male | 142631.1 | 108033.0 | 188342.4 |
| 383 | Infected with omicron | <40 | Male | 231774.4 | 175080.1 | 308191.0 |
| 71 | Infection-naïve | >40-60 | Male | 5956.2 | 4652.0 | 7671.7 |
| 51 | Infected before omicron | >40-60 | Male | 24860.5 | 16899.9 | 36185.3 |
| 76 | Infected with omicron | >40-60 | Male | 4654.5 | 3352.5 | 6529.4 |
| 374 | Infection-naïve | >40-60 | Male | 58324.4 | 46623.3 | 73005.6 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 380* | Infected before omicron | >40-60 | Male | 134217.5 | 103462.1 | 173850.3 |
| 408 | Infected with omicron | >40-60 | Male | 243767.4 | 155162.1 | 383631.1 |
| | | | | | | |
| 87 | Infection-naïve | >60 | Male | 6074.7 | 4340.2 | 8382.9 |
| 73 | Infected before omicron | >60 | Male | 17498.8 | 12260.8 | 24714.5 |
| 89 | Infected with omicron | >60 | Male | 4900.9 | 3180.0 | 7456.8 |
| 363 | Infection-naïve | >60 | Male | 67086.8 | 49747.9 | 90406.9 |
| 373 | Infected before omicron | >60 | Male | 142498.1 | 105746.3 | 194067.1 |
| 380 | Infected with omicron | >60 | Male | 228963.9 | 169009.9 | 312731.2 |

[a] The day from 1st vaccine is selected based on when the peak after the second dose and the third dose was reached according to the infection status, age group, and sex
* Neutralizing antibodies peak after the third dose did not plateau. Instead, the median days from the 12-months sampling round was selected.
CI: Confidence of interval
Source data are provided as a Source Data file

**Supplementary Table 4. Predicted mean probability of positive IgA responses, represented in percentage, in individuals after the administration first vaccination dose according to infection status, age group, and sex**

| Days from 1st vaccine [a] | Infectious status | Age Group | Sex | Geometric mean | CI 2.5% | CI 97.5% |
|---|---|---|---|---|---|---|
| 74 | Infection-naïve | <40 | Female | 67.1 | 56.3 | 76.7 |
| 64 | Infected before omicron | <40 | Female | 85.5 | 77.3 | 91.4 |
| 71 | Infected with omicron | <40 | Female | 43.5 | 28.9 | 58.8 |
| 363 | Infection-naïve | <40 | Female | 33.4 | 22.2 | 45.9 |
| 388 | Infected before omicron | <40 | Female | 82.2 | 73.2 | 89.1 |
| 418 | Infected with omicron | <40 | Female | 96.7 | 87.7 | 99.6 |
| 74 | Infection-naïve | >40-60 | Female | 64.2 | 57.0 | 71.0 |
| 62 | Infected before omicron | >40-60 | Female | 84.0 | 76.4 | 89.9 |
| 71 | Infected with omicron | >40-60 | Female | 40.2 | 27.2 | 54.4 |
| 367 | Infection-naïve | >40-60 | Female | 34.9 | 28.0 | 42.5 |
| 400 | Infected before omicron | >40-60 | Female | 84.7 | 74.7 | 91.9 |
| 428 | Infected with omicron | >40-60 | Female | 97.8 | 89.7 | 99.9 |
| 71 | Infection-naïve | >60 | Female | 43.8 | 33.6 | 54.3 |
| 53 | Infected before omicron | >60 | Female | 72.0 | 60.0 | 82.0 |
| 66 | Infected with omicron | >60 | Female | 23.4 | 13.1 | 36.4 |
| 355 | Infection-naïve | >60 | Female | 44.9 | 30.9 | 59.6 |
| 374 | Infected before omicron | >60 | Female | 86.6 | 78.2 | 92.6 |
| 405 | Infected with omicron | >60 | Female | 96.7 | 90.1 | 99.3 |
| 74 | Infection-naïve | <40 | Male | 69.2 | 56.4 | 80.1 |
| 64 | Infected before omicron | <40 | Male | 86.6 | 77.8 | 92.7 |
| 71 | Infected with omicron | <40 | Male | 45.9 | 29.8 | 62.8 |
| 364 | Infection-naïve | <40 | Male | 35.7 | 22.7 | 50.3 |
| 388 | Infected before omicron | <40 | Male | 83.5 | 73.6 | 90.7 |
| 418 | Infected with omicron | <40 | Male | 97.0 | 88.6 | 99.7 |
| 74 | Infection-naïve | >40-60 | Male | 66.4 | 55.9 | 75.5 |
| 62 | Infected before omicron | >40-60 | Male | 85.2 | 76.4 | 91.5 |
| 71 | Infected with omicron | >40-60 | Male | 42.6 | 27.8 | 58.6 |
| 368 | Infection-naïve | >40-60 | Male | 37.3 | 27.1 | 48.2 |

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|---|---|---|---|---|---|---|
| 400 | Infected before omicron | >40-60 | Male | 85.9 | 75.3 | 92.9 |
| 428 | Infected with omicron | >40-60 | Male | 98.0 | 90.5 | 99.9 |
| | | | | | | |
| 71 | Infection-naïve | >60 | Male | 46.3 | 33.6 | 59.1 |
| 53 | Infected before omicron | >60 | Male | 73.9 | 60.6 | 84.5 |
| 66 | Infected with omicron | >60 | Male | 25.3 | 13.8 | 40.0 |
| 355 | Infection-naïve | >60 | Male | 47.4 | 31.6 | 64.1 |
| 374 | Infected before omicron | >60 | Male | 87.6 | 79.0 | 93.6 |
| 406 | Infected with omicron | >60 | Male | 97.0 | 90.5 | 99.4 |

[a] The day from 1st vaccine is selected based on when the peak after the second dose and the third dose was reached according to the infection status, age group, and sex
CI: Confidence of interval
Source data are provided as a Source Data file

**Supplementary Table 5. Predicted mean IFN-γ levels, represented in mIU/ml, in individuals after the administration first vaccination dose according to infection status, age group, and sex**

| Days from 1st vaccine [a] | Infectious status | Age Group | Sex | Geometric mean | CI 2.5% | CI 97.5% |
|---|---|---|---|---|---|---|
| 210 | Infection-naïve | <40 | Female | 551.9 | 438.1 | 689.7 |
| 210 | Infected before omicron | <40 | Female | 1167.9 | 773.9 | 1771.3 |
| 210 | Infected with omicron | <40 | Female | 624.0 | 408.8 | 961.9 |
| 380 | Infection-naïve | <40 | Female | 1366.9 | 1147.6 | 1628.7 |
| 380 | Infected before omicron | <40 | Female | 3041.2 | 2380.4 | 3866.9 |
| 380 | Infected with omicron | <40 | Female | 3949.4 | 3007.7 | 5146.0 |
| 210 | Infection-naïve | >40-60 | Female | 416.2 | 340.5 | 508.0 |
| 210 | Infected before omicron | >40-60 | Female | 880.8 | 578.0 | 1325.8 |
| 210 | Infected with omicron | >40-60 | Female | 470.6 | 309.4 | 716.9 |
| 380 | Infection-naïve | >40-60 | Female | 1030.8 | 902.1 | 1175.7 |
| 380 | Infected before omicron | >40-60 | Female | 2293.4 | 1808.4 | 2914.1 |
| 380 | Infected with omicron | >40-60 | Female | 2978.4 | 2323.3 | 3826.8 |
| 210 | Infection-naïve | >60 | Female | 410.9 | 323.6 | 523.8 |
| 210 | Infected before omicron | >60 | Female | 869.4 | 559.2 | 1354.6 |
| 210 | Infected with omicron | >60 | Female | 464.5 | 297.8 | 725.3 |
| 380 | Infection-naïve | >60 | Female | 1017.6 | 844.5 | 1226.6 |
| 380 | Infected before omicron | >60 | Female | 2263.9 | 1708.0 | 3009.7 |
| 380 | Infected with omicron | >60 | Female | 2940.0 | 2180.5 | 3962.4 |
| 210 | Infection-naïve | <40 | Male | 414.7 | 288.6 | 575.1 |
| 210 | Infected before omicron | <40 | Male | 873.2 | 526.9 | 1416.8 |
| 210 | Infected with omicron | <40 | Male | 468.5 | 285.7 | 754.4 |
| 380 | Infection-naïve | <40 | Male | 1021.0 | 718.7 | 1381.1 |
| 380 | Infected before omicron | <40 | Male | 2259.8 | 1502.2 | 3198.4 |
| 380 | Infected with omicron | <40 | Male | 2929.7 | 1935.0 | 4185.4 |
| 210 | Infection-naïve | >40-60 | Male | 313.3 | 222.7 | 427.3 |
| 210 | Infected before omicron | >40-60 | Male | 659.8 | 395.8 | 1064.2 |
| 210 | Infected with omicron | >40-60 | Male | 354.0 | 217.7 | 567.3 |
| 380 | Infection-naïve | >40-60 | Male | 771.4 | 551.6 | 1016.9 |

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|---|---|---|---|---|---|---|
| 380 | Infected before omicron | >40-60 | Male | 1707.4 | 1134.3 | 2405.1 |
| 380 | Infected with omicron | >40-60 | Male | 2213.5 | 1475.0 | 3120.6 |
| | | | | | | |
| 210 | Infection-naïve | >60 | Male | 309.3 | 215.4 | 428.3 |
| 210 | Infected before omicron | >60 | Male | 651.3 | 387.7 | 1075.9 |
| 210 | Infected with omicron | >60 | Male | 349.4 | 211.9 | 568.7 |
| 380 | Infection-naïve | >60 | Male | 761.5 | 537.9 | 1027.2 |
| 380 | Infected before omicron | >60 | Male | 1685.5 | 1100.4 | 2449.6 |
| 380 | Infected with omicron | >60 | Male | 2185.1 | 1429.0 | 3165.8 |

[a] The day from 1st vaccine is selected based on the median of days from the first vaccine at 6- and 12-month rounds according to the infection status, age group, and sex
CI: Confidence of interval
Source data are provided as a Source Data file

**Supplementary Table 6. Predicted mean IgG levels, represented in AU/ml, in individuals after the administration first vaccination dose according to reinfection status, age group, and sex**

| Days from 1st vaccine [a] | Reinfection status | Age Group | Sex | Geometric mean | CI 2.5% | CI 97.5% |
|---|---|---|---|---|---|---|
| 49 | Reinfected | <40 | Female | 19670.3 | 13693.8 | 27950.8 |
| 45 | No reinfected | <40 | Female | 42971.3 | 29434.4 | 61865.0 |
| 180 | Reinfected | <40 | Female | 4099.2 | 2805.4 | 6009.9 |
| 180 | No reinfected | <40 | Female | 6783.3 | 4639.6 | 10005.2 |
| 380 | Reinfected | <40 | Female | 9692.7 | 6675.3 | 13933.5 |
| 380 | No reinfected | <40 | Female | 12584.9 | 8728.9 | 18061.7 |
| 49 | Reinfected | >40-60 | Female | 18061.4 | 12945.1 | 25069.3 |
| 45 | No reinfected | >40-60 | Female | 39456.7 | 28123.8 | 54540.4 |
| 180 | Reinfected | >40-60 | Female | 3763.9 | 2630.3 | 5337.5 |
| 180 | No reinfected | >40-60 | Female | 6228.5 | 4383.0 | 8863.4 |
| 380 | Reinfected | >40-60 | Female | 8899.9 | 6297.4 | 12378.7 |
| 380 | No reinfected | >40-60 | Female | 11555.6 | 8289.6 | 16014.8 |
| 49 | Reinfected | >60 | Female | 35661.7 | 22114.7 | 57838.5 |
| 45 | No reinfected | >60 | Female | 77905.9 | 47798.4 | 125488.4 |
| 180 | Reinfected | >60 | Female | 7431.7 | 4537.2 | 12309.1 |
| 180 | No reinfected | >60 | Female | 12298.0 | 7471.0 | 20022.9 |
| 380 | Reinfected | >60 | Female | 17572.6 | 10762.2 | 28422.8 |
| 380 | No reinfected | >60 | Female | 22816.1 | 13934.5 | 37189.7 |
| 49 | Reinfected | <40 | Male | 12404.9 | 7565.1 | 20304.0 |
| 45 | No reinfected | <40 | Male | 27099.6 | 16571.8 | 44603.3 |
| 180 | Reinfected | <40 | Male | 2585.1 | 1547.1 | 4333.5 |
| 180 | No reinfected | <40 | Male | 4277.9 | 2589.0 | 7186.0 |
| 380 | Reinfected | <40 | Male | 6112.6 | 3722.1 | 10152.7 |
| 380 | No reinfected | <40 | Male | 7936.6 | 4858.0 | 12970.9 |
| 49 | Reinfected | >40-60 | Male | 11390.3 | 7018.1 | 18370.7 |
| 45 | No reinfected | >40-60 | Male | 24883.1 | 15519.3 | 39842.7 |
| 180 | Reinfected | >40-60 | Male | 2373.7 | 1418.6 | 3922.7 |
| 180 | No reinfected | >40-60 | Male | 3928.0 | 2371.4 | 6409.4 |

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|---|---|---|---|---|---|---|
| 380 | Reinfected | >40-60 | Male | 5612.7 | 3414.2 | 9146.8 |
| 380 | No reinfected | >40-60 | Male | 7287.4 | 4512.0 | 11746.3 |
| | | | | | | |
| 49 | Reinfected | >60 | Male | 22489.8 | 12753.0 | 39385.3 |
| 45 | No reinfected | >60 | Male | 49130.8 | 28204.4 | 85464.5 |
| 180 | Reinfected | >60 | Male | 4686.8 | 2623.0 | 8426.4 |
| 180 | No reinfected | >60 | Male | 7755.6 | 4340.0 | 13659.0 |
| 380 | Reinfected | >60 | Male | 11082.0 | 6246.5 | 19648.6 |
| 380 | No reinfected | >60 | Male | 14388.8 | 8258.3 | 25183.3 |

[a] The day from 1st vaccine is selected based on the IgG peak after second dose of vaccination, waning period and at the median days from first vaccine dose at the 12-month round (as the IgG levels plateaued) according to the reinfection status, age group, and sex
CI: Confidence of interval
Source data are provided as a Source Data file

**Supplementary Table 7. Predicted mean neutralizing antibody levels, represented in IU/ml, in individuals after the administration first vaccination dose according to reinfection status, age group, and sex**

| Days from 1st vaccine [a] | Reinfection status | Age Group | Sex | Geometric mean | CI 2.5% | CI 97.5% |
|---|---|---|---|---|---|---|
| 80 | Reinfected | <40 | Female | 87550.6 | 47314.0 | 164557.3 |
| 51 | No reinfected | <40 | Female | 181644.7 | 91917.4 | 359418.3 |
| 180 | Reinfected | <40 | Female | 25015.9 | 15551.0 | 40543.6 |
| 180 | No reinfected | <40 | Female | 53698.3 | 32990.5 | 87744.7 |
| 380 | Reinfected | <40 | Female | 100232.2 | 69087.4 | 145281.7 |
| 380 | No reinfected | <40 | Female | 131254.4 | 89912.8 | 192731.6 |
| 80 | Reinfected | >40-60 | Female | 81449.2 | 44527.0 | 147529.8 |
| 51 | No reinfected | >40-60 | Female | 168985.8 | 88671.5 | 318856.5 |
| 180 | Reinfected | >40-60 | Female | 23272.5 | 14909.2 | 36358.3 |
| 180 | No reinfected | >40-60 | Female | 49956.0 | 32139.6 | 78078.9 |
| 380 | Reinfected | >40-60 | Female | 93247.0 | 67275.2 | 129474.3 |
| 380 | No reinfected | >40-60 | Female | 122107.2 | 87850.8 | 169110.2 |
| 80 | Reinfected | >60 | Female | 171591.1 | 79196.9 | 368147.1 |
| 51 | No reinfected | >60 | Female | 356007.0 | 166804.2 | 767560.8 |
| 180 | Reinfected | >60 | Female | 49028.9 | 25784.8 | 93815.8 |
| 180 | No reinfected | >60 | Female | 105243.7 | 55407.5 | 202605.7 |
| 380 | Reinfected | >60 | Female | 196446.0 | 110858.9 | 350097.5 |
| 380 | No reinfected | >60 | Female | 257246.5 | 146377.5 | 451441.5 |
| 80 | Reinfected | <40 | Male | 48864.3 | 22343.5 | 109088.4 |
| 51 | No reinfected | <40 | Male | 101380.8 | 45127.4 | 226009.9 |
| 180 | Reinfected | <40 | Male | 13962.1 | 7006.0 | 27840.6 |
| 180 | No reinfected | <40 | Male | 29970.5 | 15425.0 | 58638.6 |
| 380 | Reinfected | <40 | Male | 55942.3 | 30273.7 | 103933.0 |
| 380 | No reinfected | <40 | Male | 73256.6 | 40117.1 | 133362.6 |
| 80 | Reinfected | >40-60 | Male | 45459.0 | 20969.4 | 98205.7 |
| 51 | No reinfected | >40-60 | Male | 94315.5 | 43416.6 | 202716.3 |
| 180 | Reinfected | >40-60 | Male | 12989.0 | 6671.8 | 25438.9 |
| 180 | No reinfected | >40-60 | Male | 27881.8 | 14687.0 | 52540.7 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 380 | Reinfected | >40-60 | Male | 52043.7 | 28700.9 | 94091.8 |
| 380 | No reinfected | >40-60 | Male | 68151.3 | 38671.9 | 119777.9 |
| | | | | | | |
| 80 | Reinfected | >60 | Male | 95769.6 | 39188.8 | 236337.0 |
| 51 | No reinfected | >60 | Male | 198697.0 | 85250.8 | 469876.2 |
| 180 | Reinfected | >60 | Male | 27364.3 | 12652.1 | 60081.8 |
| 180 | No reinfected | >60 | Male | 58739.3 | 27466.4 | 124462.5 |
| 380 | Reinfected | >60 | Male | 109641.8 | 53297.7 | 224660.3 |
| 380 | No reinfected | >60 | Male | 143576.2 | 71704.9 | 288173.2 |

[a] The day from 1st vaccine is selected based on the neutralizing antibody peak after second dose of vaccination, waning period and at the median days from first vaccine dose at the 12-month round (as the neutralizing antibody levels plateaued) according to the reinfection status, age group, and sex
CI: Confidence of interval
Source data are provided as a Source Data file

**Supplementary Table 8. Predicted mean probability of positive IgA responses, represented in percentage, in individuals after the administration first vaccination dose according to reinfection status, age group, and sex**

| Days from 1st vaccine [a] | Reinfection status | Age Group | Sex | Geometric mean | CI 2.5% | CI 97.5% |
|---|---|---|---|---|---|---|
| 51 | Reinfected | <40 | Female | 94.7 | 78.7 | 99.6 |
| 45 | No reinfected | <40 | Female | 99.6 | 97.2 | 100.0 |
| 180 | Reinfected | <40 | Female | 32.4 | 5.9 | 74.0 |
| 180 | No reinfected | <40 | Female | 76.3 | 34.1 | 97.0 |
| 380 | Reinfected | <40 | Female | 84.0 | 51.4 | 98.0 |
| 380 | No reinfected | <40 | Female | 86.5 | 54.3 | 98.6 |
| 55 | Reinfected | >40-60 | Female | 97.5 | 89.6 | 99.8 |
| 47 | No reinfected | >40-60 | Female | 99.8 | 98.8 | 100.0 |
| 180 | Reinfected | >40-60 | Female | 40.2 | 11.8 | 75.4 |
| 180 | No reinfected | >40-60 | Female | 83.0 | 50.6 | 97.4 |
| 380 | Reinfected | >40-60 | Female | 79.7 | 49.3 | 95.7 |
| 380 | No reinfected | >40-60 | Female | 83.2 | 54.9 | 96.9 |
| 52 | Reinfected | >60 | Female | 87.1 | 37.6 | 99.7 |
| 46 | No reinfected | >60 | Female | 98.9 | 92.2 | 100.0 |
| 180 | Reinfected | >60 | Female | 47.0 | 3.7 | 95.2 |
| 180 | No reinfected | >60 | Female | 81.4 | 24.9 | 99.5 |
| 380 | Reinfected | >60 | Female | 94.1 | 57.9 | 100.0 |
| 380 | No reinfected | >60 | Female | 95.2 | 65.6 | 100.0 |
| 51 | Reinfected | <40 | Male | 89.3 | 52.6 | 99.6 |
| 46 | No reinfected | <40 | Male | 99.0 | 93.0 | 100.0 |
| 180 | Reinfected | <40 | Male | 25.0 | 1.6 | 77.4 |
| 180 | No reinfected | <40 | Male | 64.6 | 13.6 | 97.2 |
| 380 | Reinfected | <40 | Male | 73.5 | 22.2 | 98.1 |
| 380 | No reinfected | <40 | Male | 77.2 | 25.4 | 98.7 |
| 55 | Reinfected | >40-60 | Male | 94.2 | 71.3 | 99.8 |
| 47 | No reinfected | >40-60 | Male | 99.5 | 96.8 | 100.0 |
| 180 | Reinfected | >40-60 | Male | 30.9 | 3.0 | 80.2 |
| 180 | No reinfected | >40-60 | Male | 72.1 | 22.2 | 97.6 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 380 | Reinfected | >40-60 | Male | 67.5 | 19.2 | 96.6 |
| 380 | No reinfected | >40-60 | Male | 71.9 | 23.0 | 97.4 |
| | | | | | | |
| 53 | Reinfected | >60 | Male | 79.8 | 18.3 | 99.7 |
| 46 | No reinfected | >60 | Male | 97.7 | 82.0 | 100.0 |
| 180 | Reinfected | >60 | Male | 37.8 | 1.5 | 94.3 |
| 180 | No reinfected | >60 | Male | 72.9 | 11.7 | 99.4 |
| 380 | Reinfected | >60 | Male | 90.3 | 37.8 | 99.9 |
| 380 | No reinfected | >60 | Male | 92.0 | 46.2 | 100.0 |

[a] The day from 1st vaccine is selected based on the IgA peak after second dose of vaccination, waning period and at the median days from first vaccine dose at the 12-month round (as the probability of positive IgA responses plateaued) according to the reinfection status, age group, and sex
CI: Confidence of interval
Source data are provided as a Source Data file

**Supplementary Table 9. Predicted mean IFN-γ levels, represented in mIU/ml, in individuals after the administration first vaccination dose according to reinfection status, age group, and sex**

| Days from 1st vaccine [a] | Reinfection status | Age Group | Sex | Geometric mean | CI 2.5% | CI 97.5% |
|---|---|---|---|---|---|---|
| 210 | Reinfected | <40 | Female | 1429.6 | 673.9 | 2995.9 |
| 210 | No reinfected | <40 | Female | 4465.1 | 2252.0 | 9064.3 |
| 380 | Reinfected | <40 | Female | 2561.2 | 1460.8 | 4448.1 |
| 380 | No reinfected | <40 | Female | 4455.3 | 2601.0 | 7811.4 |
| 210 | Reinfected | >40-60 | Female | 1329.3 | 631.8 | 2766.2 |
| 210 | No reinfected | >40-60 | Female | 4151.8 | 2092.5 | 8263.8 |
| 380 | Reinfected | >40-60 | Female | 2381.5 | 1370.9 | 4117.1 |
| 380 | No reinfected | >40-60 | Female | 4142.7 | 2403.9 | 7146.2 |
| 210 | Reinfected | >60 | Female | 2604.5 | 923.4 | 7534.1 |
| 210 | No reinfected | >60 | Female | 8134.9 | 3136.2 | 21655.2 |
| 380 | Reinfected | >60 | Female | 4666.2 | 1799.7 | 11904.4 |
| 380 | No reinfected | >60 | Female | 8117.0 | 3295.7 | 19942.3 |
| 210 | Reinfected | <40 | Male | 1574.4 | 463.7 | 5304.6 |
| 210 | No reinfected | <40 | Male | 4917.3 | 1660.7 | 14774.9 |
| 380 | Reinfected | <40 | Male | 2820.6 | 943.1 | 8329.5 |
| 380 | No reinfected | <40 | Male | 4906.5 | 1747.2 | 14043.4 |
| 210 | No reinfected | >40-60 | Male | 4572.3 | 1414.1 | 14689.7 |
| 380 | No reinfected | >40-60 | Male | 4562.2 | 1511.1 | 13859.6 |
| 210 | No reinfected | >60 | Male | 8958.7 | 2420.5 | 32962.0 |
| 380 | No reinfected | >60 | Male | 8939.0 | 2504.4 | 31698.9 |

[a] The day from 1st vaccine is selected based on the median of days from the first vaccine at 6- and 12-month rounds according to the reinfection status, age group, and sex
CI: Confidence of interval
Source data are provided as a Source Data file

**Supplementary Table 10. Predicted mean IgG levels, represented in AU/ml, in individuals after the administration first vaccination dose according to future infection status, age group, and sex**

| Days from 1st vaccine [a] | Future infectious status | Age Group | Sex | Geometric mean | CI 2.5% | CI 97.5% |
|---|---|---|---|---|---|---|
| 77 | Future omicron infected | <40 | Female | 24845.6 | 20393.7 | 30119.5 |
| 79 | Infection-naïve | <40 | Female | 27074.8 | 21903.0 | 33387.8 |
| 180 | Future omicron infected | <40 | Female | 2313.5 | 1951.7 | 2752.1 |
| 180 | Infection-naïve | <40 | Female | 2455.1 | 2055.7 | 2940.3 |
| 413 | Future omicron infected | <40 | Female | 15426.4 | 11169.0 | 21507.8 |
| 389 | Infection-naïve | <40 | Female | 16404.5 | 14077.5 | 19134.0 |
| 82 | Future omicron infected | >40-60 | Female | 23369.3 | 20313.9 | 26980.0 |
| 83 | Infection-naïve | >40-60 | Female | 25712.4 | 22368.2 | 29591.7 |
| 180 | Future omicron infected | >40-60 | Female | 2032.9 | 1817.3 | 2279.0 |
| 180 | Infection-naïve | >40-60 | Female | 2157.4 | 1916.4 | 2418.3 |
| 387 | Future omicron infected | >40-60 | Female | 13081.2 | 11805.0 | 14463.9 |
| 378 | Infection-naïve | >40-60 | Female | 14948.8 | 13602.2 | 16429.2 |
| 85 | Future omicron infected | >60 | Female | 20726.7 | 17021.2 | 25161.3 |
| 86 | Infection-naïve | >60 | Female | 22921.3 | 18955.0 | 27633.6 |
| 180 | Future omicron infected | >60 | Female | 1542.6 | 1314.4 | 1807.9 |
| 180 | Infection-naïve | >60 | Female | 1637.1 | 1415.5 | 1895.1 |
| 382 | Future omicron infected | >60 | Female | 13509.9 | 11851.1 | 15409.6 |
| 375 | Infection-naïve | >60 | Female | 15615.9 | 13809.1 | 17642.4 |
| 75 | Future omicron infected | <40 | Male | 16896.3 | 12692.4 | 22432.2 |
| 78 | Infection-naïve | <40 | Male | 18342.3 | 13539.6 | 24556.6 |
| 180 | Future omicron infected | <40 | Male | 1984.6 | 1546.3 | 2576.2 |
| 180 | Infection-naïve | <40 | Male | 2106.2 | 1631.2 | 2733.3 |
| 399* | Future omicron infected | <40 | Male | 17769.2 | 12900.2 | 24430.3 |
| 399 | Infection-naïve | <40 | Male | 18906.9 | 13928.4 | 25678.5 |
| 81 | Future omicron infected | >40-60 | Male | 15773.0 | 12118.6 | 20535.6 |
| 83 | Infection-naïve | >40-60 | Male | 17330.7 | 13318.4 | 22340.0 |
| 180 | Future omicron infected | >40-60 | Male | 1743.9 | 1388.2 | 2203.3 |
| 180 | Infection-naïve | >40-60 | Male | 1850.7 | 1477.8 | 2325.4 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 395 | Future omicron infected | >40-60 | Male | 14956.9 | 11691.4 | 19085.3 |
| 382 | Infection-naïve | >40-60 | Male | 16701.0 | 14045.4 | 19846.7 |
| 85 | Future omicron infected | >60 | Male | 13951.6 | 10556.7 | 18498.6 |
| 86 | Infection-naïve | >60 | Male | 15421.6 | 11786.5 | 20116.0 |
| 180 | Future omicron infected | >60 | Male | 1323.4 | 1042.9 | 1684.0 |
| 180 | Infection-naïve | >60 | Male | 1404.4 | 1112.5 | 1756.7 |
| 387 | Future omicron infected | >60 | Male | 15243.5 | 12424.4 | 18650.1 |
| 379 | Infection-naïve | >60 | Male | 17350.1 | 14571.5 | 20749.6 |

[a] The day from 1st vaccine is selected based on the IgG peak after the second dose of vaccination, waning period and the IgG peak after the third dose of vaccination according to the reinfection status, age group, and sex

* IgG peak after the third dose did not plateau. Instead, the selected day was chosen based on the IgG peak after the third dose in the infection-naïve group to allow a direct comparison between groups

CI: Confidence of interval

Source data are provided as a Source Data file

**Supplementary Table 11. Predicted mean neutralizing antibody levels, represented in IU/ml, in individuals after the administration first vaccination dose according to future infection status, age group, and sex**

| Days from 1st vaccine [a] | Future infectious status | Age Group | Sex | Geometric mean | CI 2.5% | CI 97.5% |
|---|---|---|---|---|---|---|
| 83 | Future omicron infected | <40 | Female | 14410.4 | 10802.3 | 19255.0 |
| 85 | Infection-naïve | <40 | Female | 15710.4 | 11433.8 | 21564.4 |
| 180 | Future omicron infected | <40 | Female | 5380.2 | 4340.5 | 6686.6 |
| 180 | Infection-naïve | <40 | Female | 4602.8 | 3656.1 | 5792.9 |
| 364 | Future omicron infected | <40 | Female | 62278.5 | 48659.4 | 80607.5 |
| 367 | Infection-naïve | <40 | Female | 68806.1 | 53509.2 | 88798.3 |
| 58 | Future omicron infected | >40-60 | Female | 8786.2 | 7597.7 | 10175.2 |
| 70 | Infection-naïve | >40-60 | Female | 8914.4 | 7611.9 | 10414.4 |
| 180 | Future omicron infected | >40-60 | Female | 4705.6 | 4061.0 | 5439.9 |
| 180 | Infection-naïve | >40-60 | Female | 4025.7 | 3465.4 | 4671.5 |
| 370 | Future omicron infected | >40-60 | Female | 55018.1 | 47094.9 | 64153.0 |
| 373 | Infection-naïve | >40-60 | Female | 61277.8 | 53185.2 | 70899.1 |
| 87 | Future omicron infected | >60 | Female | 8266.8 | 6266.9 | 10948.6 |
| 88 | Infection-naïve | >60 | Female | 9041.1 | 6769.3 | 12121.5 |
| 180 | Future omicron infected | >60 | Female | 3067.7 | 2508.3 | 3748.0 |
| 180 | Infection-naïve | >60 | Female | 2624.4 | 2163.3 | 3162.9 |
| 366 | Future omicron infected | >60 | Female | 54222.4 | 43165.0 | 67953.8 |
| 369 | Infection-naïve | >60 | Female | 60114.3 | 49266.9 | 73359.1 |
| 85 | Future omicron infected | <40 | Male | 10918.9 | 7041.8 | 16840.1 |
| 87 | Infection-naïve | <40 | Male | 11926.1 | 7731.6 | 18212.8 |
| 180 | Future omicron infected | <40 | Male | 3570.2 | 2570.6 | 4990.9 |
| 180 | Infection-naïve | <40 | Male | 3054.3 | 2181.3 | 4275.1 |
| 373 | Future omicron infected | <40 | Male | 62268.7 | 46830.0 | 83486.2 |
| 375 | Infection-naïve | <40 | Male | 69519.7 | 52750.1 | 91999.4 |
| 67 | Future omicron infected | >40-60 | Male | 6233.9 | 4758.1 | 8243.8 |
| 75 | Infection-naïve | >40-60 | Male | 6586.1 | 4908.6 | 8856.1 |
| 180 | Future omicron infected | >40-60 | Male | 3122.5 | 2328.2 | 4194.0 |
| 180 | Infection-naïve | >40-60 | Male | 2671.3 | 1998.1 | 3570.9 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 383 | Future omicron infected | >40-60 | Male | 57023.2 | 44302.5 | 72917.5 |
| 384 | Infection-naïve | >40-60 | Male | 64111.1 | 50441.2 | 80947.8 |
| | | | | | | |
| 88 | Future omicron infected | >60 | Male | 6287.4 | 4214.6 | 9333.0 |
| 89 | Infection-naïve | >60 | Male | 6881.5 | 4776.9 | 9940.0 |
| 180 | Future omicron infected | >60 | Male | 2035.6 | 1494.0 | 2763.1 |
| 180 | Infection-naïve | >60 | Male | 1741.5 | 1288.9 | 2329.3 |
| 375 | Future omicron infected | >60 | Male | 54801.2 | 41925.0 | 71436.2 |
| 377 | Infection-naïve | >60 | Male | 61281.6 | 47630.3 | 78411.3 |

[a] The day from 1st vaccine is selected based on the neutralizing antibody peak after the second dose of vaccination, waning period and the neutralizing antibody peak after the third dose of vaccination according to the reinfection status, age group, and sex
CI: Confidence of interval
Source data are provided as a Source Data file

**Supplementary Table 12. Predicted mean probability of positive IgA responses, represented in percentage, in individuals after the administration first vaccination dose according to future infection status, age group, and sex**

| Days from 1st vaccine [a] | Future infectious status | Age Group | Sex | Geometric mean | CI 2.5% | CI 97.5% |
|---|---|---|---|---|---|---|
| 76 | Future omicron infected | <40 | Female | 64.7 | 54.3 | 74.2 |
| 71 | Infection-naïve | <40 | Female | 56.3 | 45.9 | 66.6 |
| 180 | Future omicron infected | <40 | Female | 5.2 | 3.1 | 8.2 |
| 180 | Infection-naïve | <40 | Female | 4.6 | 2.6 | 7.3 |
| 364 | Future omicron infected | <40 | Female | 32.2 | 22.8 | 43.1 |
| 359 | Infection-naïve | <40 | Female | 45.9 | 33.9 | 58.4 |
| 76 | Future omicron infected | >40-60 | Female | 65.5 | 57.0 | 73.5 |
| 71 | Infection-naïve | >40-60 | Female | 57.2 | 48.8 | 65.3 |
| 180 | Future omicron infected | >40-60 | Female | 5.3 | 3.4 | 7.9 |
| 180 | Infection-naïve | >40-60 | Female | 4.7 | 2.9 | 6.9 |
| 364 | Future omicron infected | >40-60 | Female | 32.9 | 24.6 | 42.2 |
| 359 | Infection-naïve | >40-60 | Female | 46.7 | 36.4 | 57.3 |
| 76 | Future omicron infected | >60 | Female | 61.4 | 51.2 | 71.2 |
| 71 | Infection-naïve | >60 | Female | 52.8 | 43.2 | 62.5 |
| 180 | Future omicron infected | >60 | Female | 4.5 | 2.7 | 7.1 |
| 180 | Infection-naïve | >60 | Female | 4.0 | 2.4 | 6.1 |
| 364 | Future omicron infected | >60 | Female | 29.2 | 20.5 | 39.1 |
| 359 | Infection-naïve | >60 | Female | 42.4 | 31.7 | 53.7 |
| 76 | Future omicron infected | <40 | Male | 62.2 | 48.6 | 74.4 |
| 71 | Infection-naïve | <40 | Male | 53.7 | 40.1 | 66.8 |
| 180 | Future omicron infected | <40 | Male | 4.8 | 2.5 | 8.1 |
| 180 | Infection-naïve | <40 | Male | 4.2 | 2.1 | 7.2 |
| 364 | Future omicron infected | <40 | Male | 30.1 | 19.0 | 43.5 |
| 359 | Infection-naïve | <40 | Male | 43.3 | 29.2 | 58.2 |
| 76 | Future omicron infected | >40-60 | Male | 63.0 | 50.8 | 74.3 |
| 71 | Infection-naïve | >40-60 | Male | 54.5 | 42.1 | 66.3 |
| 180 | Future omicron infected | >40-60 | Male | 4.9 | 2.7 | 8.2 |
| 180 | Infection-naïve | >40-60 | Male | 4.3 | 2.4 | 7.0 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 364 | Future omicron infected | >40-60 | Male | 30.7 | 20.1 | 43.2 |
| 359 | Infection-naïve | >40-60 | Male | 44.1 | 30.8 | 58.2 |
| | | | | | | |
| 76 | Future omicron infected | >60 | Male | 58.8 | 45.7 | 71.1 |
| 71 | Infection-naïve | >60 | Male | 50.2 | 37.7 | 62.6 |
| 180 | Future omicron infected | >60 | Male | 4.2 | 2.2 | 7.1 |
| 180 | Infection-naïve | >60 | Male | 3.6 | 1.9 | 6.0 |
| 364 | Future omicron infected | >60 | Male | 27.2 | 17.2 | 39.4 |
| 359 | Infection-naïve | >60 | Male | 39.9 | 27.2 | 53.8 |

[a] The day from 1st vaccine is selected based on the IgA peak after the second dose of vaccination, waning period and the IgA peak after the third dose of vaccination according to the reinfection status, age group, and sex
CI: Confidence of interval
Source data are provided as a Source Data file

**Supplementary Table 13. Predicted mean IFN-γ levels, represented in mIU/ml, in individuals after the administration first vaccination dose according to future infection status, age group, and sex**

| Days from 1st vaccine [a] | Future infectious status | Age Group | Sex | Geometric mean | CI 2.5% | CI 97.5% |
|---|---|---|---|---|---|---|
| 210 | Future omicron infected | <40 | Female | 490.0 | 358.8 | 666.5 |
| 210 | Infection-naïve | <40 | Female | 743.2 | 554.8 | 1001.0 |
| 380 | Future omicron infected | <40 | Female | 1586.6 | 1277.8 | 1959.1 |
| 380 | Infection-naïve | <40 | Female | 1519.0 | 1217.7 | 1897.5 |
| 210 | Future omicron infected | >40-60 | Female | 356.6 | 271.4 | 469.7 |
| 210 | Infection-naïve | >40-60 | Female | 540.8 | 422.1 | 697.0 |
| 380 | Future omicron infected | >40-60 | Female | 1154.6 | 981.2 | 1355.9 |
| 380 | Infection-naïve | >40-60 | Female | 1105.4 | 942.1 | 1295.0 |
| 210 | Future omicron infected | >60 | Female | 329.1 | 240.3 | 451.3 |
| 210 | Infection-naïve | >60 | Female | 499.1 | 375.5 | 664.8 |
| 380 | Future omicron infected | >60 | Female | 1065.5 | 858.6 | 1324.9 |
| 380 | Infection-naïve | >60 | Female | 1020.1 | 826.2 | 1254.5 |
| 210 | Future omicron infected | <40 | Male | 413.6 | 274.4 | 612.3 |
| 210 | Infection-naïve | <40 | Male | 627.3 | 430.0 | 912.7 |
| 380 | Future omicron infected | <40 | Male | 1339.3 | 966.5 | 1847.3 |
| 380 | Infection-naïve | <40 | Male | 1282.2 | 931.2 | 1757.3 |
| 210 | Future omicron infected | >40-60 | Male | 301.0 | 206.9 | 440.4 |
| 210 | Infection-naïve | >40-60 | Male | 456.5 | 323.8 | 642.9 |
| 380 | Future omicron infected | >40-60 | Male | 974.6 | 725.3 | 1311.8 |
| 380 | Infection-naïve | >40-60 | Male | 933.1 | 702.8 | 1225.8 |
| 210 | Future omicron infected | >60 | Male | 277.8 | 186.3 | 413.3 |
| 210 | Infection-naïve | >60 | Male | 421.3 | 294.0 | 599.7 |
| 380 | Future omicron infected | >60 | Male | 899.4 | 651.0 | 1224.2 |
| 380 | Infection-naïve | >60 | Male | 861.0 | 639.2 | 1161.4 |

[a] The day from 1st vaccine is selected based on the median of days from the first vaccine at 6- and 12-month rounds according to the future infection status, age group, and sex
CI: Confidence of interval
Source data are provided as a Source Data file

**Supplementary Table 14. Predicted mean IgG levels, represented in AU/ml, in individuals after the administration first vaccination dose according to immune imprinting status, age group, and sex**

| Days from 1st vaccine [a] | Immune imprinting status | Age Group | Sex | Geometric mean | CI 2.5% | CI 97.5% |
|---|---|---|---|---|---|---|
| 48 | Before omicron/Reinfected | <40 | Female | 45324.8 | 29493.7 | 69612.9 |
| 79 | Infected with omicron | <40 | Female | 18988.7 | 13805.5 | 26104.8 |
| 180 | Before omicron/Reinfected | <40 | Female | 7446.1 | 4552.5 | 12172.1 |
| 180 | Infected with omicron | <40 | Female | 2119.7 | 1614.2 | 2778.7 |
| 387 | Before omicron/Reinfected | <40 | Female | 19486.1 | 14070.5 | 27085.9 |
| 407 | Infected with omicron | <40 | Female | 43958.0 | 34770.3 | 55826.7 |
| 50 | Before omicron/Reinfected | >40-60 | Female | 34200.7 | 22056.5 | 53057.4 |
| 82 | Infected with omicron | >40-60 | Female | 16133.9 | 12331.2 | 21142.3 |
| 180 | Before omicron/Reinfected | >40-60 | Female | 6343.8 | 3928.3 | 10285.3 |
| 180 | Infected with omicron | >40-60 | Female | 1806.0 | 1449.3 | 2246.4 |
| 380* | Before omicron/Reinfected | >40-60 | Female | 19131.6 | 13235.0 | 27610.9 |
| 380* | Infected with omicron | >40-60 | Female | 38634.7 | 32693.9 | 45610.6 |
| 54 | Before omicron/Reinfected | >60 | Female | 32388.7 | 18224.0 | 58045.4 |
| 84 | Infected with omicron | >60 | Female | 18332.4 | 11121.5 | 30132.3 |
| 180 | Before omicron/Reinfected | >60 | Female | 6723.2 | 3551.4 | 12888.9 |
| 180 | Infected with omicron | >60 | Female | 1914.0 | 1186.4 | 3116.6 |
| 370 | Before omicron/Reinfected | >60 | Female | 22356.7 | 12961.0 | 38165.1 |
| 391 | Infected with omicron | >60 | Female | 45804.0 | 33216.4 | 63704.9 |
| 54 | Before omicron/Reinfected | <40 | Male | 33186.6 | 19098.9 | 57725.4 |
| 84 | Infected with omicron | <40 | Male | 18859.3 | 11474.1 | 31168.4 |
| 180 | Before omicron/Reinfected | <40 | Male | 6175.4 | 3361.4 | 11521.4 |
| 180 | Infected with omicron | <40 | Male | 1758.0 | 1142.7 | 2694.4 |
| 388 | Before omicron/Reinfected | <40 | Male | 16762.0 | 11344.6 | 24656.8 |
| 406 | Infected with omicron | <40 | Male | 37747.7 | 25801.2 | 54900.1 |
| 57 | Before omicron/Reinfected | >40-60 | Male | 25880.1 | 14648.6 | 45472.8 |
| 86 | Infected with omicron | >40-60 | Male | 16175.4 | 9853.7 | 26517.6 |
| 180 | Before omicron/Reinfected | >40-60 | Male | 5261.3 | 2956.7 | 9611.8 |
| 180 | Infected with omicron | >40-60 | Male | 1497.8 | 1036.5 | 2172.7 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 380* | Before omicron/Reinfected | >40-60 | Male | 16424.6 | 10752.0 | 25210.8 |
| 380* | Infected with omicron | >40-60 | Male | 33168.3 | 25168.4 | 43779.3 |
| | | | | | | |
| 67 | Before omicron/Reinfected | >60 | Male | 26519.4 | 12448.4 | 57851.3 |
| 87 | Infected with omicron | >60 | Male | 18539.3 | 9778.0 | 35430.8 |
| 180 | Before omicron/Reinfected | >60 | Male | 5575.9 | 2740.7 | 11333.2 |
| 180 | Infected with omicron | >60 | Male | 1587.4 | 920.7 | 2748.9 |
| 372 | Before omicron/Reinfected | >60 | Male | 19109.1 | 11053.1 | 32924.1 |
| 391 | Infected with omicron | >60 | Male | 39413.6 | 27149.5 | 57548.4 |

[a] The day from 1st vaccine is selected based on the IgG levels at the waning period and the IgG peak after the third dose of vaccination according to the immune imprinting status, age group, and sex

* IgG peak after the third dose did not plateau. Instead, the median days from the 12-months sampling round was selected.

CI: Confidence of interval

Source data are provided as a Source Data file

**Supplementary Table 15. Predicted mean neutralizing antibody levels, represented in IU/ml, in individuals after the administration first vaccination dose according to immune imprinting status, age group, and sex**

| Days from 1st vaccine [a] | Immune imprinting status | Age Group | Sex | Geometric mean | CI 2.5% | CI 97.5% |
|---|---|---|---|---|---|---|
| 43 | Before omicron/Reinfected | <40 | Female | 146500.6 | 47648.5 | 452401.5 |
| 83 | Infected with omicron | <40 | Female | 8980.3 | 6587.0 | 12319.2 |
| 180 | Before omicron/Reinfected | <40 | Female | 36049.4 | 19569.4 | 66900.2 |
| 180 | Infected with omicron | <40 | Female | 4210.8 | 3153.6 | 5590.6 |
| 403* | Before omicron/Reinfected | <40 | Female | 161599.8 | 90048.9 | 284183.1 |
| 403 | Infected with omicron | <40 | Female | 278283.8 | 204666.8 | 371499.7 |
| 43 | Before omicron/Reinfected | >40-60 | Female | 117992.6 | 38568.2 | 365904.0 |
| 83 | Infected with omicron | >40-60 | Female | 7232.8 | 5411.6 | 9592.6 |
| 180 | Before omicron/Reinfected | >40-60 | Female | 29034.4 | 15705.8 | 53990.1 |
| 180 | Infected with omicron | >40-60 | Female | 3391.4 | 2618.2 | 4380.3 |
| 403* | Before omicron/Reinfected | >40-60 | Female | 130153.6 | 72007.4 | 229584.5 |
| 403 | Infected with omicron | >40-60 | Female | 224131.8 | 169729.8 | 291023.5 |
| 43 | Before omicron/Reinfected | >60 | Female | 135619.4 | 43189.7 | 426974.0 |
| 83 | Infected with omicron | >60 | Female | 8313.3 | 5445.4 | 12675.0 |
| 180 | Before omicron/Reinfected | >60 | Female | 33371.8 | 16936.2 | 65804.7 |
| 180 | Infected with omicron | >60 | Female | 3898.0 | 2596.4 | 5869.2 |
| 403* | Before omicron/Reinfected | >60 | Female | 149597.1 | 77403.9 | 284571.3 |
| 403 | Infected with omicron | >60 | Female | 257614.5 | 168280.0 | 392277.1 |
| 43 | Before omicron/Reinfected | <40 | Male | 128061.0 | 41250.3 | 404999.9 |
| 83 | Infected with omicron | <40 | Male | 7850.0 | 5308.2 | 11658.5 |
| 180 | Before omicron/Reinfected | <40 | Male | 31512.0 | 16282.9 | 61206.7 |
| 180 | Infected with omicron | <40 | Male | 3680.8 | 2520.0 | 5365.1 |
| 403* | Before omicron/Reinfected | <40 | Male | 141259.7 | 75906.2 | 261823.8 |
| 403 | Infected with omicron | <40 | Male | 243257.1 | 163183.8 | 353462.1 |
| 43 | Before omicron/Reinfected | >40-60 | Male | 103141.2 | 33055.9 | 321986.2 |
| 83 | Infected with omicron | >40-60 | Male | 6322.4 | 4334.0 | 9181.2 |
| 180 | Before omicron/Reinfected | >40-60 | Male | 25380.0 | 13009.4 | 49711.3 |
| 180 | Infected with omicron | >40-60 | Male | 2964.5 | 2071.0 | 4230.0 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 403* | Before omicron/Reinfected | >40-60 | Male | 113771.6 | 60643.6 | 212204.3 |
| 403 | Infected with omicron | >40-60 | Male | 195921.0 | 135413.2 | 281352.3 |
| | | | | | | |
| 43 | Before omicron/Reinfected | >60 | Male | 118549.4 | 37259.9 | 381681.1 |
| 83 | Infected with omicron | >60 | Male | 7267.0 | 4552.6 | 11676.3 |
| 180 | Before omicron/Reinfected | >60 | Male | 29171.4 | 14075.5 | 60326.6 |
| 180 | Infected with omicron | >60 | Male | 3407.4 | 2151.4 | 5425.5 |
| 403* | Before omicron/Reinfected | >60 | Male | 130767.7 | 66128.0 | 260162.2 |
| 403 | Infected with omicron | >60 | Male | 225189.3 | 138798.4 | 361099.7 |

[a] The day from 1st vaccine is selected based on the neutralizing antibody levels at the waning period and the neutralizing antibody peak after the third dose of vaccination according to the immune imprinting status, age group, and sex

* Neutralizing antibody peak after the third dose did not plateau. Instead, the selected day was chosen based on the neutralizing antibody peak after the third dose in the "infected with omicron" group to allow a direct comparison between groups

CI: Confidence of interval

Source data are provided as a Source Data file

**Supplementary Table 16. Predicted mean probability of positive IgA responses, represented in percentage, in individuals after the administration first vaccination dose according to immune imprinting status, age group, and sex**

| Days from 1st vaccine [a] | Immune imprinting status | Age Group | Sex | Geometric mean | CI 2.5% | CI 97.5% |
|---|---|---|---|---|---|---|
| 58 | Before omicron/Reinfected | <40 | Female | 95.6 | 80.0 | 99.7 |
| 71 | Infected with omicron | <40 | Female | 39.5 | 20.5 | 61.6 |
| 180 | Before omicron/Reinfected | <40 | Female | 43.1 | 10.8 | 81.6 |
| 180 | Infected with omicron | <40 | Female | 1.5 | 0.3 | 4.8 |
| 410 | Before omicron/Reinfected | <40 | Female | 90.7 | 62.4 | 99.3 |
| 415 | Infected with omicron | <40 | Female | 98.4 | 93.5 | 99.8 |
| 59 | Before omicron/Reinfected | >40-60 | Female | 94.9 | 75.9 | 99.7 |
| 71 | Infected with omicron | >40-60 | Female | 35.5 | 19.5 | 54.5 |
| 180 | Before omicron/Reinfected | >40-60 | Female | 39.5 | 8.8 | 79.3 |
| 180 | Infected with omicron | >40-60 | Female | 1.3 | 0.2 | 4.0 |
| 411 | Before omicron/Reinfected | >40-60 | Female | 89.3 | 58.0 | 99.3 |
| 415 | Infected with omicron | >40-60 | Female | 98.2 | 93.0 | 99.8 |
| 62 | Before omicron/Reinfected | >60 | Female | 80.8 | 32.7 | 98.8 |
| 71 | Infected with omicron | >60 | Female | 11.2 | 2.3 | 31.1 |
| 180 | Before omicron/Reinfected | >60 | Female | 14.4 | 1.3 | 50.3 |
| 180 | Infected with omicron | >60 | Female | 0.3 | 0.0 | 1.4 |
| 436 | Before omicron/Reinfected | >60 | Female | 69.1 | 6.0 | 99.6 |
| 421 | Infected with omicron | >60 | Female | 91.3 | 63.7 | 99.4 |
| 57 | Before omicron/Reinfected | <40 | Male | 98.1 | 89.8 | 99.9 |
| 71 | Infected with omicron | <40 | Male | 63.3 | 34.7 | 86.5 |
| 180 | Before omicron/Reinfected | <40 | Male | 64.1 | 21.5 | 94.1 |
| 180 | Infected with omicron | <40 | Male | 4.2 | 0.7 | 13.1 |
| 407 | Before omicron/Reinfected | <40 | Male | 95.7 | 79.2 | 99.8 |
| 415 | Infected with omicron | <40 | Male | 99.3 | 96.8 | 100.0 |
| 58 | Before omicron/Reinfected | >40-60 | Male | 97.7 | 88.2 | 99.9 |
| 71 | Infected with omicron | >40-60 | Male | 59.6 | 33.1 | 82.5 |
| 180 | Before omicron/Reinfected | >40-60 | Male | 60.8 | 18.8 | 92.9 |
| 180 | Infected with omicron | >40-60 | Male | 3.5 | 0.6 | 10.9 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 408 | Before omicron/Reinfected | >40-60 | Male | 95.1 | 75.6 | 99.7 |
| 415 | Infected with omicron | >40-60 | Male | 99.2 | 96.5 | 100.0 |
| | | | | | | |
| 60 | Before omicron/Reinfected | >60 | Male | 90.3 | 54.7 | 99.6 |
| 71 | Infected with omicron | >60 | Male | 25.1 | 5.5 | 58.9 |
| 180 | Before omicron/Reinfected | >60 | Male | 29.1 | 3.2 | 76.3 |
| 180 | Infected with omicron | >60 | Male | 0.9 | 0.1 | 3.6 |
| 416 | Before omicron/Reinfected | >60 | Male | 81.9 | 29.2 | 99.3 |
| 419 | Infected with omicron | >60 | Male | 96.2 | 81.4 | 99.8 |

[a] The day from 1st vaccine is selected based on the probability of positive IgA responses at the waning period and the probability of positive IgA responses peak after the third dose of vaccination according to the immune imprinting status, age group, and sex
CI: Confidence of interval
Source data are provided as a Source Data file

**Supplementary Table 17. Predicted mean IFN-γ levels, represented in mIU/ml, in individuals after the administration first vaccination dose according to immune imprinting status, age, and sex**

| Days from 1st vaccine [a] | Immune imprinting status | Age Group | Sex | Geometric mean | CI 2.5% | CI 97.5% |
|---|---|---|---|---|---|---|
| 210 | Before omicron/Reinfected | <40 | Female | 5260.2 | 1498.3 | 18145.3 |
| 210 | Infected with omicron | <40 | Female | 641.9 | 413.7 | 989.9 |
| 380 | Before omicron/Reinfected | <40 | Female | 4950.7 | 2821.8 | 8806.2 |
| 380 | Infected with omicron | <40 | Female | 4172.8 | 2984.6 | 5846.8 |
| 210 | Before omicron/Reinfected | >40-60 | Female | 4545.6 | 1314.1 | 15632.8 |
| 210 | Infected with omicron | >40-60 | Female | 554.7 | 374.5 | 831.7 |
| 380 | Before omicron/Reinfected | >40-60 | Female | 4278.1 | 2387.0 | 7862.2 |
| 380 | Infected with omicron | >40-60 | Female | 3606.0 | 2748.5 | 4750.4 |
| 210 | Before omicron/Reinfected | >60 | Female | 3435.1 | 907.7 | 12539.5 |
| 210 | Infected with omicron | >60 | Female | 419.2 | 211.8 | 830.4 |
| 380 | Before omicron/Reinfected | >60 | Female | 3232.9 | 1462.8 | 7323.2 |
| 380 | Infected with omicron | >60 | Female | 2725.0 | 1478.0 | 5008.4 |
| 210 | Before omicron/Reinfected | <40 | Male | 3919.6 | 1025.9 | 14779.1 |
| 210 | Infected with omicron | <40 | Male | 478.3 | 270.4 | 845.3 |
| 380 | Before omicron/Reinfected | <40 | Male | 3688.9 | 1808.2 | 7645.5 |
| 380 | Infected with omicron | <40 | Male | 3109.3 | 1896.9 | 5067.6 |
| 210 | Infected with omicron | >40-60 | Male | 413.3 | 238.6 | 720.0 |
| 380 | Infected with omicron | >40-60 | Male | 2686.9 | 1687.7 | 4235.0 |
| 210 | Infected with omicron | >60 | Male | 312.4 | 149.2 | 668.0 |
| 380 | Infected with omicron | >60 | Male | 2030.5 | 1014.9 | 4022.6 |

[a] The day from 1st vaccine is selected based on the median of days from the first vaccine at 6- and 12-month rounds according to the future infection status, age group, and sex
CI: Confidence of interval
Source data are provided as a Source Data file

**Supplementary Table 18. Multiple linear regression analysis for IgG, IgA, neutralizing antibody (nAb), and IFN-γ levels associations with sex, age, time from last vaccine dose administrated or infection, and the infection status in the different cohorts studied (reinfected, future infection, and immune imprinting cohorts). Data are expressed in log10(AU/ml) for IgG and IgA, log10(IU/ml) for nAb, and log10(mIU/ml) for IFN-γ.**

| Reinfected cohort | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | IgG log10(AU/ml) | | | IgA log10(AU/ml) | | | Neutralizing antibodies log10(IU/ml) | | | IFN-γ log10(mIU/ml) [a] | | |
| **Variable** | **Estimate** | **Std. Error** | **p-value** | **Estimate** | **Std. Error** | **p-value** | **Estimate** | **Std. Error** | **p-value** | **Estimate** | **Std. Error** | **p-value** |
| Intercept [b] | 4.8925 | 0.0721 | <2e-16*** | 3.2943 | 0.2227 | <2e-16*** | 5.5116 | 0.1515 | <2e-16*** | N.A. | N.A. | N.A. |
| Age, >40–60 years old | 0.0021 | 0.0646 | 0.9731 | 0.0081 | 0.1995 | 0.9677 | -0.0770 | 0.1348 | 0.5688 | N.A. | N.A. | N.A. |
| Age, >60 years old | 0.2428 | 0.1018 | 0.0188* | -0.0464 | 0.3143 | 0.8829 | 0.0600 | 0.2114 | 0.7772 | N.A. | N.A. | N.A. |
| Sex, male | -0.1175 | 0.0929 | 0.2089 | -0.2162 | 0.2868 | 0.4525 | -0.3792 | 0.1930 | 0.0522 | N.A. | N.A. | N.A. |
| Time from second vaccine dose (days) | -0.0068 | 0.0006 | <2e-16*** | -0.0140 | 0.0020 | 4.06e-10*** | -0.0064 | 0.0014 | 2.14e-05*** | N.A. | N.A. | N.A. |
| Reinfected status, Reinfected | -0.2072 | 0.0592 | 0.0006*** | -0.3766 | 0.1826 | 0.0416* | -0.2647 | 0.1240 | 0.0351* | N.A. | N.A. | N.A. |
| **Future infection cohort** | | | | | | | | | | | | |
| | IgG log10(AU/ml) | | | IgA log10(AU/ml) | | | Neutralizing antibodies log10(IU/ml) | | | IFN-γ log10(mIU/ml) | | |
| **Variable** | **Estimate** | **Std. Error** | **p-value** | **Estimate** | **Std. Error** | **p-value** | **Estimate** | **Std. Error** | **p-value** | **Estimate** | **Std. Error** | **p-value** |
| Intercept [c] | 4.7117 | 0.0655 | <2e-16*** | 2.1513 | 0.2151 | <2e-16*** | 5.4289 | 0.0896 | <2e-16*** | 3.4840 | 0.1473 | <2e-16*** |
| Age, >40–60 years old | 0.0040 | 0.0318 | 0.8982 | 0.1915 | 0.1045 | 0.0672 | 0.0190 | 0.0435 | 0.662 | -0.1373 | 0.0637 | 0.0316* |
| Age, >60 years old | 0.0261 | 0.0363 | 0.4715 | 0.2623 | 0.1192 | 0.0281 | 0.0134 | 0.0497 | 0.787 | -0.2491 | 0.0737 | 0.0007*** |
| Sex, male | 0.0677 | 0.0362 | 0.0617 | -0.1195 | 0.1189 | 0.3150 | 0.0513 | 0.0497 | 0.302 | -0.0376 | 0.0733 | 0.6077 |
| Time from booster (days) | -0.0066 | 0.0007 | <2e-16*** | -0.0128 | 0.0024 | 2.17e-07*** | -0.0078 | 0.0010 | 5.25e-14*** | -0.0040 | 0.0017 | 0.0220* |
| Future infected status, Infected | -0.0574 | 0.0241 | 0.0178* | -0.1635 | 0.0793 | 0.0397* | -0.0541 | 0.0331 | 0.103 | 0.0061 | 0.0497 | 0.9023 |

| Immune imprinting cohort | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | IgG log10(AU/ml) | | | IgA log10(AU/ml) | | | Neutralizing antibodies log10(IU/ml) | | | IFN-γ log10(mIU/ml) | | |
| **Variable** | **Estimate** | **Std. Error** | **p-value** | **Estimate** | **Std. Error** | **p-value** | **Estimate** | **Std. Error** | **p-value** | **Estimate** | **Std. Error** | **p-value** |
| Intercept [d] | 4.1268 | 0.0777 | <2e-16*** | 1.8431 | 0.2366 | 5.32e-13*** | 4.9596 | 0.1241 | <2e-16*** | 3.6388 | 0.1638 | <2e-16*** |
| Age, >40–60 years old | 0.0156 | 0.0480 | 0.7445 | -0.0038 | 0.1462 | 0.9788 | 0.0084 | 0.0767 | 0.9125 | -0.0892 | 0.0926 | 0.337 |
| Age, >60 years old | 0.0419 | 0.0763 | 0.5834 | -0.2714 | 0.2325 | 0.2445 | 0.0567 | 0.1243 | 0.6486 | -0.1697 | 0.1543 | 0.274 |
| Sex, male | -0.1125 | 0.0565 | 0.0482* | 0.0811 | 0.1722 | 0.6379 | -0.0782 | 0.0904 | 0.3881 | -0.1128 | 0.1104 | 0.309 |
| Time from last infection (days) | 0.0078 | 0.0018 | 2.19-0.5*** | 0.0203 | 0.0054 | 0.0002*** | 0.0086 | 0.0028 | 0.0031* | 0.0037 | 0.0055 | 0.507 |
| Infected status, Infected with Omicron | 0.3069 | 0.0683 | 1.25e-05*** | 0.4394 | 0.2079 | 0.0359* | 0.2106 | 0.1090 | 0.0549* | -0.0565 | 0.1362 | 0.679 |

[a] Intercept defined as a <40 years old female individual, not reinfected, with IgG/IgA/nAb/IFN-γ levels at 14 days after the administration of the second dose
[b] Intercept defined as a <40 years old female individual, not future infected, with IgG/IgA/nAb/IFN-γ levels at 14 days after the administration of the third dose
[a] Intercept defined as a <40 years old female individual, infected before Omicron and reinfected, with IgG/IgA/nAb/IFN-γ levels at 0 days after last infection
* p<0.05, ** p<0.01, **** p<0.0001 (two-sided p-values were calculated using multiple linear regression analysis). p<0.05 was considered significant.
N.A.: Not applicable, small size group
Source data are provided as a Source Data file

## Supplementary References


1. Hansen, C. B. *et al.* SARS-CoV-2 Antibody Responses Are Correlated to Disease Severity in COVID-19 Convalescent Individuals. *J. Immunol.* **206**, 109–117 (2021).

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3. Brooks, M. *et al.* glmmTMB Balances Speed and Flexibility Among Packages for Zero-inflated Generalized Linear Mixed Modeling. *R J.* **9**, 378–400 (2017).

4. Pérez-Alós, L. *et al.* Modeling of waning immunity after SARS-CoV-2 vaccination and influencing factors. *Nat. Commun.* **13**, 1614 (2022).