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SciScore Report

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Table 1: Rigor Adherence Table

Ethics
Consent: Participants provided electronic consent upon enrolment.
Inclusion and Exclusion Criteria
Study participants:For this investigation, we included participants who provided two blood samples after receiving only two mRNA vaccines of the same type (either two doses of BNT162b2, or two doses of mRNA-1273 vaccines).
Attrition
not detected.
Sex as a biological variable
The various factors included in the model were: participant age (years, continuous variable), female sex at birth (vs. male); “racialized” (including those who self-described their ethnicity or race as South Asian, Chinese, Black, Filipina, Latin American, Arab, Southeast Asian, West Asian, Korean, or Japanese) (vs. whites)”; “BMI: 18.5 to <25kg/m2 (vs. others)”, “BMI ≥ 25kg/m2 (vs others)”; “BNT162b2 vaccine (vs. mRNA-1273)”; “short vaccine dosing interval (binary variable, “short” defined as a vaccine dosing interval less than the median value); and past medical history (including covariates: hypertension, diabetes, asthma, liver diseases, and cancer).
Subject Demographics
Weight: The various factors included in the model were: participant age (years, continuous variable), female sex at birth (vs. male); “racialized” (including those who self-described their ethnicity or race as South Asian, Chinese, Black, Filipina, Latin American, Arab, Southeast Asian, West Asian, Korean, or Japanese) (vs. whites)”; “BMI: 18.5 to <25kg/m2 (vs. others)”, “BMI ≥ 25kg/m2 (vs others)”; “BNT162b2 vaccine (vs. mRNA-1273)”; “short vaccine dosing interval (binary variable, “short” defined as a vaccine dosing interval less than the median value); and past medical history (including covariates: hypertension, diabetes, asthma, liver diseases, and cancer).
Randomization
not detected.
Blinding
not detected.

Power Analysis
not detected.
Replication
not required.
Data Information
Availability: Data Summary statement: Due to the confidential nature of participants blood samples used for this study, the data cannot be published publicly but would be made available upon reasonable request.

Table 2: Key Resources Table

Your Sentences	REAGENT or RESOURCE	SOURCE	IDENTIFIER
Antibodies			
Serological Testing:We tested all samples with: (1) Elecsys Anti-SARS-CoV-2 (nucleocapsid) [Roche Diagnostics International Ltd, Rotkreuz, Switzerland] assay20,21 to confirm eligibility; (2) the quantitative Roche Elecsys Anti-SARS-CoV-2 (S) (Roche Diagnostics International Ltd, Rotkreuz, Switzerland) assay for measuring spike total antibody concentrations; and (3) the Meso Scale Discovery (MSD) V-PLEX COVID-19 Coronavirus Panel 2 IgG assay for measuring IgG to spike and receptor-binding domain (RBD) antigens.	Anti-SARS-CoV-2 (nucleocapsid)		
	Anti-SARS-CoV-2		
	receptor-binding domain (RBD) antigens.		
Study outcomes:The primary outcome was total anti-spike antibody concentrations (measured with the Elecsys assay), and the secondary outcomes were IgG concentrations to spike and RBD antigens (measured with the VPLEX assay).	anti-spike		
Antibody concentrations (including: total anti-spike, anti-spike IgG and anti-RBD IgG antibody concentrations) were presented as geometric mean (GM) with corresponding geometric standard deviations (GSD).	anti-spike, anti-spike IgG		
	anti-RBD IgG		

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Materials Design Analysis Reporting (MDAR) Checklist for Authors

The MDAR framework establishes a minimum set of requirements in transparent reporting applicable to studies in the life sciences (see Statement of Task: doi:10.31222/osf.oio/9sm4x.). The MDAR checklist is a tool for authors, editors and others seeking to adopt the MDAR framework for transparent reporting in manuscripts and other outputs. Please refer to the MDAR Elaboration Document for additional context for the MDAR framework.

Materials

Antibodies	Yes (indicate where provided: page no/section/legend)	n/a
For commercial reagents, provide supplier name, catalogue number and RRID, if available	Yes, 6 antibodies detected, 0 RRID provided : Anti-SARS-CoV-2 (nucleocapsid) : Anti-SARS-CoV-2 : receptor-binding domain (RBD) antigens. : anti-spike : anti-spike, anti-spike IgG : anti-RBD IgG Please add identifiers for all resources where possible	

Cell Materials	Yes (indicate where provided: page no/section/legend)	n/a
Cell lines: Provide species information, strain. Provide accession number in repository OR supplier name, catalog number, clone number, OR RRID	No cell lines detected Please add identifiers for all resources where possible	
Primary cultures: Provide species, strain, sex of origin, genetic modification status.	Not currently checked by SciScore	

Experimental Animals	Yes (indicate where provided: page no/section/legend)	n/a
Laboratory animals: Provide species, strain, sex, age, genetic modification status. Provide accession number in repository OR supplier name, catalog number, clone number, OR RRID	No organisms detected Please add identifiers for all resources where possible	
Animal observed in or captured from the field: Provide species, sex and age where possible	Not currently checked by SciScore	
Model organisms: Provide Accession number in repository (where relevant) OR RRID	See laboratory animals section for information.	

Plants and microbes	Yes (indicate where provided: page no/section/legend)	n/a
Plants: provide species and strain, unique accession number if available, and source (including location for collected wild specimens)	Not currently checked by SciScore	
Microbes: provide species and strain, unique accession number if available, and source	Not currently checked by SciScore	

Human research participants	Yes (indicate where provided: page no/section/legend)	n/a
Identify authority granting ethics approval (IRB or equivalent committee(s), provide reference number for approval.	Not detected.	
Provide statement confirming informed consent obtained from study participants.	Participants provided electronic consent upon enrolment.	
Report on age and sex for all study participants.	**Age:**Not detected. **Sex:**The various factors included in the model were: participant age (years, continuous variable), female sex at birth (vs. male); “racialized” (including those who self-described their ethnicity or race as South Asian, Chinese, Black, Filipina, Latin American, Arab, Southeast Asian, West Asian, Korean, or Japanese) (vs. whites)”; “BMI: 18.5	

Human research participants	Yes (indicate where provided: page no/section/legend)	n/a
	to <25kg/m2 (vs. others)", "BMI **Sex:≥Sex:** 25kg/m2 (vs others)"; "BNT162b2 vaccine (vs. mRNA-1273)"; "short vaccine dosing interval (binary variable, "short" defined as a vaccine dosing interval less than the median value); and past medical history (including covariates: hypertension, diabetes, asthma, liver diseases, and cancer).	

Design

Study protocol	Yes (indicate where provided: page no/section/legend)	n/a
For clinical trials, provide the trial registration number OR cite DOI in manuscript.	Not detected.	

Laboratory protocol	Yes (indicate where provided: page no/section/legend)	n/a
Provide DOI or other citation details if detailed step-by-step protocols are available.	Not detected.	

Experimental study design (statistics details)	Yes (indicate where provided: page no/section/legend)	n/a
State whether and how the following have been done, or if they were not carried out		
Sample size determination	not detected.	
Randomization	not detected.	
Blinding	not detected.	
inclusion/exclusion criteria	Study participants:For this investigation, we included participants who provided two blood samples after receiving only two mRNA vaccines of the same type (either two doses of BNT162b2, or two doses of mRNA-1273 vaccines).	

Sample definition and in-laboratory replication	Yes (indicate where provided: page no/section/legend)	n/a
State number of times the experiment was replicated in laboratory	Not detected.	
Define whether data describe technical or biological replicates	Not detected.	

Ethics	Yes (indicate where provided: page no/section/legend)	n/a
Studies involving human participants: State details of authority granting ethics approval (IRB or equivalent committee(s), provide reference number for approval.	Not detected.	
Studies involving experimental animals: State details of authority granting ethics approval (IRB or equivalent committee(s), provide reference number for approval.	Not detected.	
Studies involving specimen and field samples: State if relevant permits obtained, provide details of authority approving study; if none were required, explain why.	Not detected.	

Dual Use Research of Concern (DURC)	Yes (indicate where provided: page no/section/legend)	n/a
If study is subject to dual use research of concern, state the authority granting approval and reference number for the regulatory approval	Not currently checked by SciScore	

Analysis

Attrition	Yes (indicate where provided: page no/section/legend)	n/a
State if sample or data point from the analysis is excluded, and whether the criteria for exclusion were determined and specified in advance.	not detected.	

Statistics	Yes (indicate where provided: page no/section/legend)	n/a
Describe statistical tests used and justify choice of tests.	Not detected.	

Data availability	Yes (indicate where provided: page no/section/legend)	n/a
State whether newly created datasets are available, including protocols for access or restriction on access.	Data Summary statement: Due to the confidential nature of participants blood samples used for this study, the data cannot be published publicly but would be made available upon reasonable request.	
If data are publicly available, provide accession number in repository or DOI or URL.	Not detected.	
If publicly available data are reused, provide accession number in repository or DOI or URL, where possible.	Not detected.	

Code availability	Yes (indicate where provided: page no/section/legend)	n/a
For all newly generated code and software essential for replicating the main findings of the study:		
State whether the code or software is available.	Not detected.	
If code is publicly available, provide accession number in repository, or DOI or URL.	Not detected.	

Analysis

Adherence to community standards	Yes (indicate where provided: page no/section/legend)	n/a
MDAR framework recommends adoption of discipline-specific guidelines, established and endorsed through community initiatives. Journals have their own policy about requiring specific guidelines and recommendations to complement MDAR.		
State if relevant guidelines (eg., ICMJE, MIBBI, ARRIVE) have been followed, and whether a checklist (eg., CONSORT, PRISMA, ARRIVE) is provided with the manuscript.	Not currently checked by SciScore	

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By Michael Asamoah-Boaheng

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11-month SARS-CoV-2 immunogenicity decay, and associated factors, among mRNA vaccinees: Implications for Booster Vaccination

--Manuscript Draft--

11-month SARS-CoV-2 immunogenicity decay, and associated factors, among mRNA vaccinees: Implications for Booster Vaccination

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Abstract

Background: We examined the 11-month longitudinal antibody decay among 2-dose mRNA vaccinees, and identified factors associated with faster decay.

Methods: The study included samples from the CORSIP longitudinal observational study of paramedics in Canada. Participants were included if they had received two mRNA vaccines without prior SARS-CoV-2 infection and provided two blood samples post-vaccination. The outcomes of interest were quantitative SARS-CoV-2 antibody concentrations. We employed spaghetti and scatter plots (with kernel-weighted local polynomial smoothing curve) to describe the trend of the antibody decay over 11-months post vaccine and fit a mixed effect exponential decay model to examine the loss of immunogenicity and factors associated with antibody waning over time.

Results: This analysis included 652 blood samples from 326 adult paramedics. Total anti-spike antibody levels peaked on the 21st day (antibody level 9,042U/mL) after the second mRNA vaccine dose. Total anti-spike antibody levels declined thereafter, with a half-life of 94 [95% CI: 70, 143] days, with levels plateauing at 295 days (antibody level 1021 U/mL). Older age, vaccine dosing interval <35 days, and the BNT162b2 vaccine (compared to mRNA-1273 vaccine) were associated with faster antibody decay.

Conclusion: Antibody levels declined after the initial mRNA series with a half-life of 94 days, plateauing at 295 days. These findings may inform the timing of booster vaccine doses and identifying individuals with faster antibody deday.

Keywords: SARS-CoV-2; Immunogenicity decay; Risk factors; antibody levels, mRNA COVID-19 vaccines.

Introduction

Data from observational studies and randomized controlled trials have demonstrated the effectiveness of COVID-19 vaccines against symptomatic illness, COVD-19-related hospitalizations, complications, and death[1–3,4]. However, the long-term duration of vaccine-induced immunity is unclear. Previous studies document waning of SARS-CoV-2 antibody levels after both vaccination and infection,[5] with anti-spike levels decreasing substantially as early as three months after the second BNT162b2 dose[6]. Humoral responses have been shown to be significantly decreased six months after the receipt of the second dose of BNT162b2 vaccine, especially among older adults (≥ 65 years) and those with compromised immune systems[6–11]. However, data on the long-term (>6 month) immunogenicity post-SARS-CoV-2 vaccination remain scarce.[6,7,10,11].

Given evidence of waning SARS-CoV-2 humoral immune responses after vaccination, booster vaccinations have been implemented in many jurisdictions; however, the optimal timing for boosters remains unclear. There is growing evidence that SARS-CoV-2 antibody levels provide a measure of COVID-19 risk[12–14] and COVID-19 severity,[15–17] a relationship that has been shown to be present even within the Omicron era[18]. Thus, antibody levels may inform decisions regarding the optimal timing of a booster vaccination. Further, given that immunity has been shown to differ based on individual characteristics, it is possible that the optimal booster schedule may vary within different patient groups. Currently there is limited data showing the long-term durability of, and factors associated with, antibody levels post-vaccination. We sought to investigate antibody waning 11 months after two mRNA vaccine doses among adult COVID-naïve paramedics in Canada, and factors associated with these outcomes.

Methods

Study setting, design, and ethics

Our study included samples of paramedics from the Occupational Risks, Seroprevalence, and Immunity among Paramedics in Canada (CORSIP) study[19]. CORSIP is a longitudinal observational study investigating the seroprevalence of SARS-CoV-2 antibodies among adult (≥ 19 years) Canadian paramedics. Participants provided blood samples and data from structured questionnaires on vaccination and COVID-19 history, past medical history, demographic and workplace characteristics.

Study participants

For this investigation, we included participants who provided two blood samples after receiving only two mRNA vaccines of the same type (either two doses of BNT162b2, or two doses of mRNA-1273 vaccines). We excluded participants who had evidence of prior SARS-CoV-2 infection at any time prior to the second blood collection, based on reported positive nucleic acid amplification viral testing or a reactive blood sample on the Elecsys Nucleocapsid Anti-SARS-CoV-2 [Roche, IND, USA] assay.[20]

Serological Testing

We tested all samples with: (1) Elecsys Anti-SARS-CoV-2 (nucleocapsid) [Roche Diagnostics International Ltd, Rotkreuz, Switzerland] assay[20,21] to confirm eligibility; (2) the quantitative Roche Elecsys Anti-SARS-CoV-2 (S) (Roche Diagnostics International Ltd, Rotkreuz, Switzerland) assay for measuring spike total antibody concentrations; and (3) the Meso Scale

Discovery (MSD) V-PLEX COVID-19 Coronavirus Panel 2 IgG assay for measuring IgG to spike and receptor-binding domain (RBD) antigens.

Study outcomes

The primary outcome was total anti-spike antibody concentrations (measured with the Elecsys assay), and the secondary outcomes were IgG concentrations to spike and RBD antigens (measured with the VPLEX assay).

Statistical analysis

We described continuous variables with mean and standard deviation (SD) for near normally distributed variables without any influential outliers, or median (with interquartile range [IQR]) for skewed or non-normally distributed variables. Categorical variables were described with counts and percentages. Antibody concentrations (including: total anti-spike, anti-spike IgG and anti-RBD IgG antibody concentrations) were presented as geometric mean (GM) with corresponding geometric standard deviations (GSD). We described the longitudinal changes in SARS-COV-2 antibodies 11 months after the second mRNA vaccine dose with scatter (with Kernel-weighted local polynomial smoothing curve)[22,23] and spaghetti plots. Using the Kernel-weighted local polynomial smoothing approach with Epanechnikov kernel function[22], we generated the smoothing values and their corresponding smoothing grids and estimated the peak antibody concentration based on the maximum kernel-weighted values. The smoothing grid (days after the second vaccine) that corresponded to the maximum kernel-weighted smoothing value was considered as the day of the peak antibody level. We used the double exponential decay (DED) model[24] to determine the time at which the antibody level stopped declining (the "plateau level") [See supplementary material].

To further demonstrate differences in antibody levels after vaccination, we categorized samples into quartiles based on the number of days they were collected after the second vaccine dose, and plotted box-and-whisker plots to diagram antibody levels.

We modeled the persistence of antibody levels over time using a mixed effect exponential decay (ED) model. The mean structure of the exponential decay model with random intercept and slope is given by:

$$log_{10}(Ab_{i,j}) = (\beta_0 + b_{0i}) + (\beta_1 + b_{1i}).T_{i,j} + \varepsilon_{i,j}$$

β_0 and β_1 are the fixed effects intercept and decay rate respectively, while b_{0i} and b_{1i} are the subject-specific (random effects) intercept and decay rates respectively. $\varepsilon_{i,j}$ represents the random error term for participant 'i' at time (day) "j" which is assumed to be normally distributed; $log_{10}(Ab_{i,j})$ is the mean log antibody titer at time $T_{i,j}$ post vaccination[9,25]. To determine the waning of antibody levels over time, we used the mixed effects ED model to estimate the half-life (the time the peak antibody level was reduced by 50%)[9] . Thus, the half-life ($t_{1/2}$) was estimated as[25]:

$$t_{1/2} = \frac{log_{10}(0.5)}{\beta_1}$$

Further, we fit a mixed effect ED model to investigate the factors associated with antibody decay over the 11-month study observation period. The mixed effect ED model with random intercept was used to account for the repeated measurements of antibody concentrations for each participant at the two different time points. This model has been used in other studies that investigated antibody waning among vaccinated individuals over time[9,25].The various factors

included in the model were: participant age (years, continuous variable), female sex at birth (vs. male); "racialized" (including those who self-described their ethnicity or race as South Asian, Chinese, Black, Filipina, Latin American, Arab, Southeast Asian, West Asian, Korean, or Japanese) (vs. whites)"; "BMI: 18.5 to <25kg/m^2 (vs. others)", "BMI ≥25kg/m^2 (vs others)"; "BNT162b2 vaccine (vs. mRNA-1273)"; "short vaccine dosing interval (binary variable, "short" defined as a vaccine dosing interval less than the median value); and past medical history (including covariates: hypertension, diabetes, asthma, liver diseases, and cancer).

Results

The study included 652 samples from 326 paramedics, with a mean age was 42 (SD=11) years, where 46% were female. The majority of the study participants (82%) were vaccinated with two doses of BNT162b2 vaccine while the remaining 18% received two doses of mRNA-1273.

Table 1 shows patient characteristics, intervals between vaccines and blood collection dates, and outcome measures. The first and second blood collection occurred at a median of 59 (IQR 29, 94) and 156 (IQR 145, 176) days after the second vaccine dose, respectively. The GM (GSD) of the total anti-spike antibody concentration at the first and second blood collection was 2940 (3.5) U/mL and 1455 (2.4) U/mL, respectively; for anti-spike IgG was 102,051(3.1) AU/mL and 30,956 (2.0) AU/mL, and for anti-spike RBD was 66,986 (3.8) AU/mL and 17,406 (2.3) AU/mL, respectively.

Figures 1 (spaghetti plots) and 2 (scatter plots, with smooth curve), and Supplementary Figure S1 (box plots), describe the longitudinal changes in antibody concentrations during the 11 months after the second vaccine. The peak values for total anti-spike (9,042 U/mL), anti-spike IgG (323,980 AU/mL), and anti-RBD IgG (249,051 AU/mL) antibody concentrations were all

recorded on the 21st day after the second vaccine dose (Figure 2 and supplementary Table S1). On the 288th day after vaccination, total anti-spike antibody levels stopped declining, plateauing at 1021 U/mL (Figure 2 and supplementary Table S1) which was 11% of the peak value. Anti-spike IgG and Anti-RBD IgG levels plateaued at 321 days (5.3% of the peak value) and 308 days (4.8% of the peak value) days post-vaccination, respectively (see supplementary Tables S1-S4).

The mixed-effects ED model identified several independent factors associated with a faster 11-month rate of post-vaccine anti-spike total antibody decay (Table 3), including: older age, a vaccine dosing interval < 35 days, and BNT162b2 (vs. mRNA-1273) vaccine type. Results examining outcomes of anti-spike and anti-RBD IgG antibody concentrations were largely consistent, except: (1) shorter vaccine dosing interval which was not significantly associated with anti-spike and anti-RBD IgG antibody decay over time; and, (2) BMI was not associated with total anti-spike antibody decay, however was associated with anti-spike and anti-RBD IgG antibody decay.

The half-lives of the total antibody, anti-spike IgG, and anti-spike RBD concentrations were 94 (95% CI: 70-143) days, 68 (95% CI: 56-89) days, and 61 (95% CI: 49-79) days respectively (Table 2).

Discussion

We investigated long-term immunogenicity from serially-tested middle-aged double-mRNA vaccinees over 11 months after receiving the second vaccine. Antibody concentrations reached maximum levels on day 21 after the second dose, subsequently declined with a half-life of 94

days, and then plateaued at a level of 1021U/mL after approximately 10 months. We found older age, a vaccine dosing interval <35 days, and the BNT162b2 (vs. mRNA-1273) vaccine to be associated with a faster rate of post-vaccination total anti-spike antibody decay. These data may assist decision makers with the timing of booster vaccination doses. Modification of vaccination schedules may be warranted for those shown to have faster antibody decay, including older individuals, those with a shorter vaccine dosing interval, and those who received the BNT162b2 vaccine. It may also be warranted to prioritize mRNA-1273 dosing for groups that are at greater risk for rapid antibody decay.

Previous studies have investigated post-vaccine antibody decay up to six months after the second vaccine dose, and as well as the factors associated with antibody decline. A longitudinal study involving vaccinated healthcare personnel recorded a rapid decline of antibody levels one month after receiving their second vaccine dose[26]. In a study that investigated the safety and immunogenicity of two mRNA-based COVID-19 vaccines, the immune response after receiving two doses of BNT162b2 was lower in the older individuals (65-85 years) than the younger age group (18 to 55 years). Perez-Alos et al[8] modelled the waning of immunity after SARS-CoV-2 vaccination for up to 230 days after the first dose and found decay of antibody levels over time. Additionally, their study found a decrease in antibody levels among older individuals (more than 60 years) independent of previous infection. These findings are consistent with our study which demonstrates faster antibody decay among older individuals after receiving two mRNA vaccine doses. This data, in combination with previous evidence shows that older individuals are more likely to have severe COVID-19[27,28], and thus, supports consideration of earlier booster vaccination strategies (which have been incorporated into some clinical recommendations [29–31]).

Our results showed that patients vaccinated with BNT162b2, vs. mRNA-1273, demonstrated a faster post-vaccine antibody decay, which may have implications for booster dose timing. Previous studies have shown a similar differences between these vaccines, including mRNA-1273 demonstrating higher humoral immunogenicity,[32] and a lower risk of breakthrough infections and COVID-19 related hospitalizations[33]. We also found extended mRNA vaccine dosing intervals '≥ 35 days' to be associated with a slower rate of antibody decay, which is congruent with previous investigations demonstrating improved immunogenicity and vaccine effectiveness with longer, compared to standard, vaccine dosing intervals[34–36,37].

The optimal timing of booster vaccination remains unclear, with some advocating for annual COVID-19 vaccines[38]. Given the existing evidence demonstrating that SARS-CoV-2 antibody levels are associated with COVID-19 risk[12–14] and disease COVID-19 severity,[15–17] antibody models may play a role in informing booster vaccination strategies. Our 11-month data indicates that antibody levels peak within 1 month, and then decline up to approximately 10 months. It is therefore unclear if an annual booster campaign will provide adequate protection and this will at least partially depend on whether SARS-CoV-2 will become primarily associated with seasonal infections.

Limitations

This observation study has several limitations. There may be additional confounding variables affecting immunogenicity decay that we did not account for. Our study participants included middle-aged paramedics in Canada; results may differ in other patient populations. Antibody levels have been shown to be associated with COVID-19 clinical outcomes, however, remain surrogate markers of immunity, and thus actual clinical outcomes may differ.

Conclusion

SARS-CoV-2 immunogenicity peaked within 21 days after the second mRNA vaccine, and subsequently declined, plateauing at approximately 10 months after the second dose. Older age, shorter vaccine dosing interval (< 35 days), and the BNT162b2 vaccine were associated with a faster rate of post-vaccination antibody decay. These findings may inform booster frequency, including patient-specific schedules.

Conflict of interest

The authors declare no conflict of interest.

Funding:

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Author contribution

Conceptualization: M.A-B, B.G, D.G, M.E.K, T.K, P.M.L, S.S, S.J.D, S.F.O, V.B, A.C.M, A.J, D.G. *Data curation*: M.A-B, B.G, D.G, T.K. *Formal analysis*: M.A-B, B.G, D.G, M.E.K, T.K, P.M.L, S.S, S.J.D, S.F.O, V.B, A.C.M, A.J, D.G. *Funding acquisition*: B.G, D.G, T.K, M.A-B. *Investigation*: M.A-B, B.G, D.G, M.E.K, T.K, P.M.L, S.S, S.J.D, S.F.O, V.B, A.C.M, A.J, D.G. Methodology: M.A-B, B.G, D.G, T.K, M.E.K. *Project administration*: B.G, D.G, T.K.

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Ethical approval

The study was approved by the University of British Columbia (H20-03620), and University of Toronto (40435) research ethics boards. Participants provided electronic consent upon enrolment.

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FIGURE LEGENDS

Figure 1: Spaghetti plots of longitudinal changes in antibody concentrations 11 months after 2 mRNA vaccine doses

Figure 2: Scatter plots (*with kernel-weighted local polynomial smoothing curve*) of longitudinal changes in antibody concentrations 11 months after 2 mRNA vaccine dose.

*Vertical lines indicate the time the peak antibody level was recorded, and the time at which the antibody levels plateaued; **horizontal lines indicate the peak antibody level and the value the antibody levels plateaued respectively

Table 1: Participants characteristics

Variables	N (%) or Mean (SD) or Median (IQR)
Baseline characteristics	**N = 326 (*at baseline*)**
Age, years, mean (SD)	42 (11)
Female Sex (at birth), n (%)	151 (46)
Racialized	25 (7.7)
Body Mass Index (BMI), mean (SD)	27 (5.0)
Obesity (≥ 30 Kg/m^2), n (%)	88 (27)
Tobacco use, n (%)	13 (4.0)
Medical History, n (%)	
Hypertension	30 (9.2)
Diabetes	5.0 (1.5)
Asthma	55 (17)
Chronic Lung Disease	3.0 (0.9)
Heart diseases	1.0 (0.3)
Kidney diseases	1.0 (0.3)
Liver disease	5.0 (1.5)
Cancer	7.0 (2.1)
Vaccine type, n (%)	
Pfizer (BNT162b2)	268 (82)
Moderna (mRNA-1273)	60 (18)
Vaccine doses, n (%)	
1st & 2nd doses (BNT162b2)	266 (82)
1st & 2nd doses (mRNA-1273)	60 (18)
Vaccine dosing Interval (days), Median (IQR)	35 (28, 42)
Time related variables	
BC 1 date, median (IQR)	2021/04/16 (2021/03/11, 2021/06/02)
BC 2 date, median (IQR)	2021/07/17 (2021/07/09, 2021/08/25)
BC_1-to-BC_2 interval (days), Median (IQR)	100 (76, 132)
V_2-to-BC_1 interval (days), Median (IQR)	59 (29, 94)
V_2-to-BC_2 interval (days), Median (IQR)	156 (145, 176)
Outcome variables (at follow-up)	
Quantitative Antibody Concentrations, GM (GSD)	
Blood Collection 1	
Anti-Spike total antibody concentration	2940 (3.5)
Anti-Spike IgG concentration	102051(3.1)
Anti-RBD IgG concentration	66986 (3.8)
Blood Collection 2	
Anti-Spike total antibody concentration	1455 (2.4)
Anti-Spike IgG concentration	30956 (2)
Anti-RBD IgG concentration	17406 (2.3)

SD: Standard deviation; gMean: geometric mean; gSD: geometric standard deviation; IQR: Interquartile range; BC1, first blood collection date; BC2, second blood collection date; V_2 : Second vaccine dose date; Vaccine dosing interval, the number of days between V1 and V2; *Racialized*: means other non-white races including Asian ethnic groups, blacks, and others.

Table 2: Estimated half-life

Models	Random Intercept (95% CI)	Adjusted decay rates, β (95% CI) (Days after vaccine 2)	Half-life (95% CI)
Model 1	2.54e-14 (0.00)	-0.0032 (-0.0043, -0.0021)	94 (70, 143)
Model 2	0.17 (0.15, 0.20)	-0.0044 (-0.0054, 0.0034)	68 (56, 89)
Model 3	0.25 (0.21, 0.29)	-0.0049 (-0.0062, -0.0038)	61 (49, 79)

All models adjusted for age, vaccine type (BNT162b2 vs mRNA-1273), Sex at birth (Female vs Male), race (Racialized vs white), tobacco use, vaccine dosing interval, BMI:18.5-25Kg/m^2; "BMI: <18.5 Kg/m^2"; underweight, and medical history (hypertension, diabetes, asthma, and Cancer)

Outcome variable for model 1 is Total Anti-spike Antibody Concentration;

Outcome variable for model 2 is Anti-Spike IgG Antibody Concentration;

Outcome variable for model 3 is Anti-RBD IgG Antibody Concentration

Table 3: Mixed effect modelling of changes in antibody concentrations 11 months after second dose

Variables	Model 1: Total Anti-Spike Antibody β (95% CI)	Model 2: Anti-Spike IgG β (95% CI)	Model 3: Anti-RBD IgG β (95% CI)
Fixed effects			
Days after the second dose	-0.0032 (-0.0043, -0.0021)*	-0.0044 (-0.0054, 0.0034)*	-0.0049 (-0.0061, -0.0038)*
Female sex (vrs Male sex)	-0.0046 (-0.11, 0.11)	-0.033 (-0.13, 0.064)	0.0024 (-0.12, 0.12)
Current age (years)	-0.0060 (-0.011, -0.00058)*	-0.0079 (-0.013, -0.0031)*	-0.0070 (-0.013, -0.0012)*
Racialized (vrs white)	-0.0097 (-0.18, 0.16)	0.085 (-0.057, 0.23)	0.073 (-0.099, 0.24)
(BMI: 18.5 to <25 kg/m^2) vs (others)	-0.20 (-0.49, 0.093)	0.21 (0.0054, 0.41)*	0.23 (-0.015, 0.48)
(BMI ≥25kg/m^2) vs Others	-0.0073 (-0.29, 0.28)	0.37 (0.15, 0.58)*	0.38 (0.13, 0.64)*
Tobacco use	-0.16 (-0.42, 0.11)	-0.12 (-0.32, 0.085)	-0.12 (-0.37, 0.12)
Vaccine type (BNT162b2 vrs mRNA-1273)	-0.30 (-0.44, -0.17)*	-0.15 (-0.27, -0.031)*	-0.21 (-0.36, -0.066)*
Shorter Dose 1-to-Dose 2 interval (<35 days)	-0.29 (-0.40, -0.18)*	0.022 (-0.076, 0.12)	-0.075 (-0.19, 0.044)
Medical History			
Hypertension	-0.18 (-0.38, 0.0088)	-0.0062 (-0.16, 0.15)	-0.038 (-0.22, 0.15)
Diabetes	-0.047 (-0.47, 0.38)	-0.078 (-0.46, 0.30)	-0.066(-0.52, 0.39)
Asthma	0.077 (-0.061, 0.21)	0.10 (-0.019, 0.23)	0.13 (-0.021., 0.27)
Liver disease	-0.082 (-0.51, 0.34)	0.013 (-0.36, 0.39)	-0.00088 (-0.46, 0.45)
Cancer	-0.14 (-0.50, 0.22)	0.033 (-0.28, 0.35)	-0.012 (-0.40, 0.37)
Random component			
Intercept/constant (95% CI)	2.54e-14 (0)	0.17 (0.15, 0.20)	0.25 (0.21, 0.29)

β (95% CI): Effects estimate (95% Confidence interval); **β** values estimates were shown to 2 significant figures; p values were shown to 3 decimal places, se: standard error; BMI: Body Mass Index (Kg/m^2).

*** = P<0.05**

SUPPLEMENTARY MATERIALS

Supplementary Methods

The Double exponential decay (DED) model is expressed mathematically as:

$$Ab_{levels} = Plateau + SpanFast * \mathbf{exp}(-\mathbf{KFast} * \mathbf{T}) + \mathbf{SpanSlow} * \mathbf{exp}(-\mathbf{KSlow} * \mathbf{T})$$

Where, $SpanFast = (Y_0 - plateau) * PercentFast * \mathbf{0.01}$

$$SpanSlow = (Y_0 - Plateau) * (\mathbf{100} - PercentFast) * \mathbf{0.01}$$

Y_0 is antibody levels ($\mathbf{Ab}_{levels}$) when the time "**T**" is zero. The ***Plateau*** is the antibody level at the infinite times; ***KFast*** and ***KSlow*** are the two rate constants expressed as the inverse of the time "**T**" in the x-axis; ***TauFast*** and ***TauSlow*** are the two-time constants and they are estimated as the inverse of the rate constants (i.e. **1/KFast** and **1/Kslow**).

Half-life (fast) and ***Half-life (slow)*** are the time units of the Time "**T**" and are computed as (**ln2/K**); and ***PercentFast*** is the fraction of the **span** (defined as the distance between Y_0 and ***Plateau*** point)[24].

Supplementary Figures

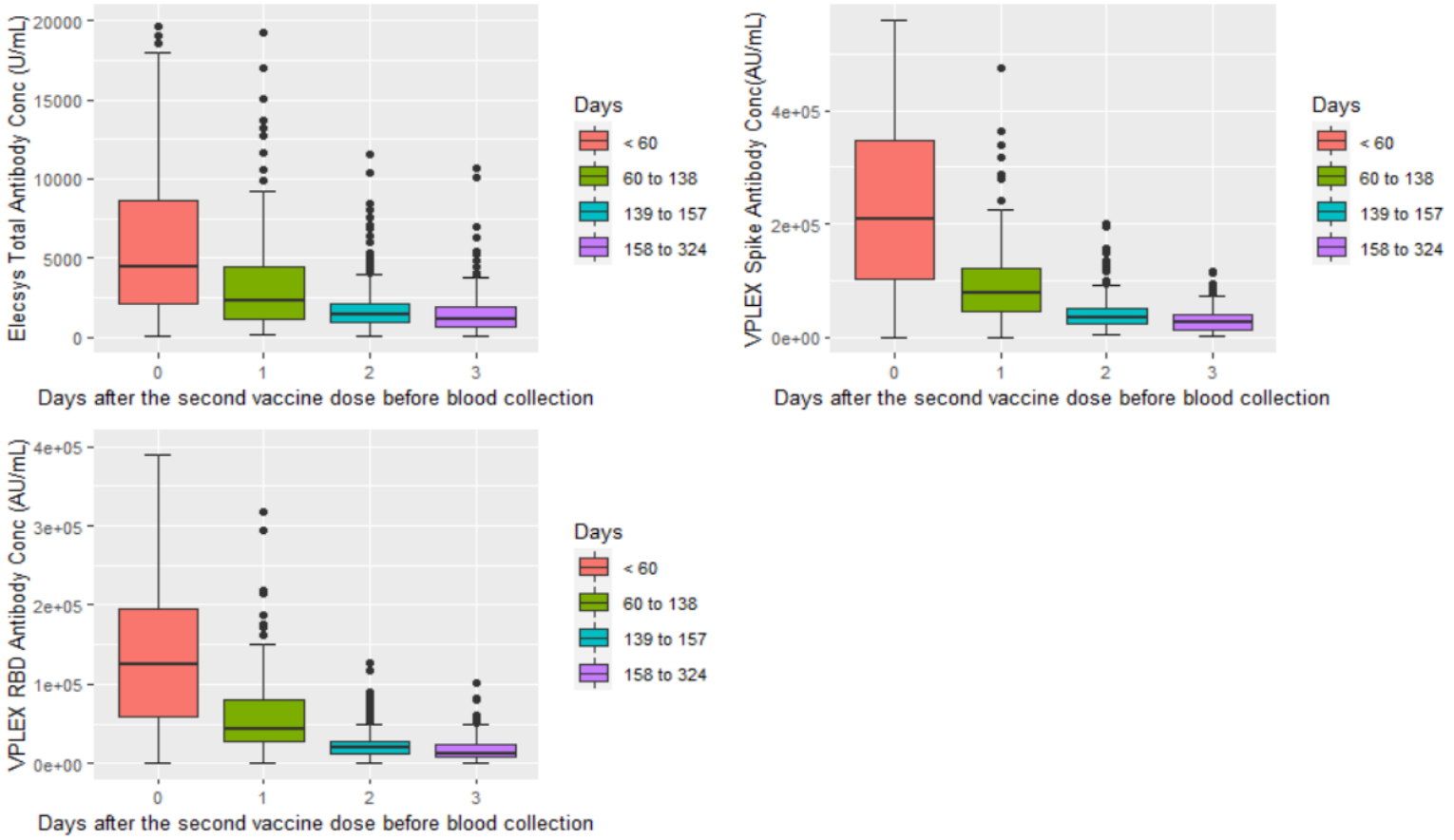

Figure S1: Box and whisker plot of antibody concentration decay by days after second vaccine (categorized into four quartiles)

Supplementary Tables

Table S1: Estimated peak antibody concentrations

Antibody concentration	Peak antibody value	Day (P)	Plateau value	Day (L)
Total Anti-Spike Antibody concentration	9,042	21	1021	288
Anti-Spike IgG Concentration	323,980	21	17287	321
Anti-RBD IgG Concentration	249,051	21	11909	308

Day (P): the day the peak antibody levels were recorded; *Day (L)*: the day/time the lowest antibody level was recorded. Lowest IgG value defined as the value equal to when the antibody levels declined to less than 5% of the peak antibody value.

Table S2: Table showing results from the DED for Total antibody concentration (U/mL)

Two phase decay	
Best-fit values	
Y0	9741
Plateau	**1021**
PercentFast	77.73
KFast	0.01835
KSlow	0.007189
Half Life (Slow)	96.42
Half Life (Fast)	37.78
Tau (slow)	139.1
Tau (fast)	54.51
Rate constant ratio	2.552
Goodness of Fit	
Robust Sum of Squares	32.63
RSDR	320.0
Constraints	
PercentFast	0 < PercentFast < 100
KFast	KFast > 1*KSlow
KSlow	KSlow > 0

Table S3: Table showing results from the DED model for anti-spike IgG (AU/mL)

Two phase decay	Hit constraint
Best-fit values	
Y0	311950
Plateau	**17287**
PercentFast	~ 25.43
KFast	~ 0.01488
KSlow	0.01488
Half Life (Slow)	46.58
Half Life (Fast)	~ 46.58
Tau (slow)	67.21
Tau (fast)	~ 67.21
Rate constant ratio	~ 1.000
Goodness of Fit	
Robust Sum of Squares	40.60
RSDR	6108
Constraints	
PercentFast	0 < PercentFast < 100
KFast	KFast > 1*KSlow
KSlow	KSlow > 0

Table S4: Table showing results from the DED model for anti-RBD IgG (AU/mL)

Two phase decay	
Best-fit values	
Y0	244272
Plateau	**11909**
PercentFast	86.06
KFast	0.01716
KSlow	0.01716
Half Life (Slow)	40.40
Half Life (Fast)	40.40
Tau (slow)	58.29
Tau (fast)	58.29
Rate constant ratio	1.000
Goodness of Fit	
Robust Sum of Squares	37.81
RSDR	5875
Constraints	
PercentFast	0 < PercentFast < 100
KFast	KFast > 1*KSlow
KSlow	KSlow > 0

Figure 1

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Figure 2

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