Journal of Microbiology, Immunology and Infection 57 (2024) 554—563

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Original Article

# Effectiveness and evolution of anti-SARS-CoV-2 spike protein titers after three doses of COVID-19 vaccination in people with HIV☆

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☆ The preliminary data of the present study have been presented in a poster presentation form (abstract no. 1020) in *Conference on Retroviruses and Opportunistic Infections* (CROI) 2023, Seattle, US, 19—22, February, 2023.

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https://doi.org/10.1016/j.jmii.2024.02.004

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Received 1 September 2023; received in revised form 20 January 2024; accepted 16 February 2024
Available online 26 February 2024

**KEYWORDS**
Serologic response;
Humoral immunity;
Immunogenicity;
mRNA-1273 vaccine;
BNT162b2 vaccine;
Booster vaccination

**Abstract** *Background:* Real-world vaccine effectiveness following the third dose of vaccination against SARS-CoV-2 remains less investigated among people with HIV (PWH).
*Methods:* PWH receiving the third dose of BNT162b2 and mRNA-1273 (either 50- or 100-μg) were enrolled. Participants were followed for 180 days until the fourth dose of COVID-19 vaccination, SARS-CoV-2 infection, seroconversion of anti-nucleocapsid IgG, death, or loss to follow-up. Anti-spike IgG was determined every 1—3 months.
*Results:* Of 1427 participants undergoing the third-dose COVID-19 vaccination, 632 (44.3%) received 100-μg mRNA-1273, 467 (32.8%) 50-μg mRNA-1273, and 328 (23.0%) BNT162b2 vaccine and the respective rate of SARS-CoV-2 infection or seroconversion of anti-nucleocapsid IgG was 246.1, 280.8 and 245.2 per 1000 person-months of follow-up (log-rank test, $p = 0.28$). Factors associated with achieving anti-S IgG titers >1047 BAU/mL included CD4 count <200 cells/mm$^3$ (adjusted odds ratio [aOR], 0.11; 95% CI, 0.04—0.31), plasma HIV RNA >200 copies/mL (aOR, 0.27; 95% CI, 0.09—0.80), having achieved anti-spike IgG >141 BAU/mL within 3 months after primary vaccination (aOR, 3.69; 95% CI, 2.68—5.07), receiving BNT162b2 vaccine as the third dose (aOR, 0.20; 95% CI, 0.10—0.41; reference, 100-μg mRNA-1273), and having previously received two doses of mRNA vaccine in primary vaccination (aOR, 2.46; 95% CI, 1,75-3.45; reference, no exposure to mRNA vaccine).
*Conclusions:* PWH receiving different types of the third dose of COVID-19 vaccine showed similar vaccine effectiveness against SARS-CoV-2 infection. An additional dose with 100-μg mRNA-1273 could generate a higher antibody response than with 50-μg mRNA-1273 and BNT162b2 vaccine.


## Introduction

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection (COVID-19) continues to spread worldwide, which has caused detrimental impacts on the access to health-care system for the general population and people with HIV (PWH).[1,2] Previous studies have demonstrated that PWH receiving two doses of COVID-19 vaccine could generate good immune responses, which could confer protection against SARS-CoV-2 infection.[3—8] However, waning immunity and breakthrough infections after the completion of two-dose primary vaccination may occur, especially in the emergence of B.1.1.529 (Omicron) variant.[9—12]

There was a consensus that all PWH should receive the full series of three doses of COVID-19 vaccine available through approval or emergency use authorization by the U.S. FDA, regardless of CD4 count or plasma HIV RNA load (PVL).[13—15] In addition, the U.S. CDC also announced that people with advanced HIV infection or those who are not taking antiretroviral therapy (ART) should get an additional primary dose.[16] However, the safety and effectiveness of these vaccines are rarely investigated among PWH.

In Taiwan, national SARS-CoV-2 vaccination program was implemented in the spring of 2021, when a community outbreak caused by the B.1.1.7 (alpha) variant took place.[17,18] For those who had received two doses of SARS-CoV-2 vaccine, a booster dose was recommended six months after the primary vaccination, including 50-μg mRNA-1273 vaccine, 30-μg BNT162b2 vaccine and 15-μg MVC-COV1901 vaccine.[19—21] Moreover, an additional dose, including 100-μg mRNA-1273 vaccine, 30-μg BNT162b2 vaccine, or 15-μg MVC-COV1901 vaccine, was also provided free-of-charge to PWH one month after the primary dose by following the recommendations of the World Health Organization.[22,23] In this prospective, observational study, we aimed to investigate the real-world effectiveness of COVID-19 vaccination and their serological responses in PWH after receiving the different types of the third doses of mRNA COVID-19 vaccine.

## Methods

### Study population and setting

This prospective cohort study was conducted at the National Taiwan University Hospital (NTUH) to include PWH aged 20 years or older who had been receiving HIV care as outpatients. Those planning to receive the third dose of SARS-

CoV-2 vaccine (either the additional primary dose or the booster dose) between June 2021 and May 2022 were enrolled. We only included PWH who received mRNA-1273 and BNT162b2 vaccine as the third dose in this study. Determinations of anti-SARS-CoV-2 spike (anti-S) IgG titers were performed every one to three months, depending on the out-patient appointments made for HIV care. All participants were followed for 180 days until receipt of the fourth dose of SARS-CoV-2 vaccine, occurrence of SARS-CoV-2 infection, seroconversion of anti-N IgG, loss to follow-up, or death, whichever occurred first. Those who had had a history of confirmed SARS-CoV-2 infection were excluded. All serum samples were also tested for anti-SARS-CoV-2 nucleocapsid (anti-N) IgG and those tested positive at baseline or during follow-up were excluded from the subsequent analysis. Medical information of the participants on the electronic medical records were reviewed, which included age, gender, body mass index, date of vaccination, CD4 count and PVL at vaccination, ART, and underlying diseases that might interfere immune responses, such as type 2 diabetes mellitus (DM), chronic kidney disease (CKD) of stage 3—5 (defined as an estimated glomerular filtration rate less than 60 mL/min/1.73m$^2$), malignancy, autoimmune disease, and viral hepatitis. For the participants who were enrolled in our previous study after two doses of SARS-CoV-2 vaccination, we also retrieved the data of anti-S and anti-N level within 3 months after they received the second dose of vaccination.[11] The study was approved by the Research Ethics Committee of the hospital (NTUH 202106149RIND) and all participants gave written informed consent.

### Laboratory investigations

The procedure of determinations of serological responses to vaccination was described in our previous study, which analyzed the sequentially collected serum samples from 1189 PLWH who had undergone two homologous primary vaccination.[11] In brief, anti-S IgG in serum samples were determined using SARS-CoV-2 IgG II Quant assay (Abbott, Abbott Park, Illinois, U.S.A.), and an anti-S IgG titer greater than 50 arbitrary units per milliliter (AU/mL) was considered positive. The mathematical relationship of the Abbott AU/mL unit to WHO unit (binding antibody unit per mL [BAU/mL]) was as follows: BAU/mL = 0.142*AU/mL, according to the manufacturer's instruction. In addition, anti-N IgG was determined using Elecsys® Anti-SARS-CoV-2 assay (Roche, U.S.A), while an anti-N IgG titer higher than 1.0 cutoff index was considered reactive.

### Outcome assessment

Primary end points included the acquisition of SARS-CoV-2 infection within 180 days after the participants had received the third dose of SARS-CoV-2 vaccine. The history of symptomatic infection was retrieved from the National Notification System for Infectious Diseases, while asymptomatic infection was defined as seroconversion of anti-N IgG in the absence of clinical symptoms. We also analyzed the serological responses within the first 16 weeks after the third dose of SARS-CoV-2 vaccination because our previous study has demonstrated that acquired immunity from primary SARS-CoV-2 infection waned within 4—7 months in COVID-19 patients.[24] In order to estimate the potential vaccine effectiveness through antibody measurements, cut-off value of 141, 1047, 6000 and 20000 BAU/mL of anti-S IgG were used. Dimeglio et al. have demonstrated that an anti-S antibody titer greater than 141 BAU/mL was associated with the presence of neutralizing antibodies through the investigation of 8758 health-care workers.[25] In addition, Stærke et al. demonstrated that those with an anti-S IgG titer greater than 1,047 BAU/mL had a risk reduction of 0.71 for breakthrough infection with the B.1.617.2 (Delta) variant, compared with those with an anti-S IgG titer less than 59 BAU/mL.[26] Moreover, Dimeglio et al. have demonstrated that an anti-S IgG of 6000—20,000 BAU/mL provided 55.6% protection, and >20,000 BAU/mL provided 87.7% protection against Omicron BA.1 infection.[27]

In order to speculate on the association between the titer of anti-S IgG and acquisition of SARS-CoV-2 infection, we compared the anti-S IgG determined 0—3 months after the vaccination between those who acquired SARS-CoV-2 infection and those did not 3—6 months after the vaccination. IgG titers determined before the third dose of vaccination and after the participants acquired SARS-CoV-2 infection remained excluded from analyses.

### Statistical analysis

Categorical variables were compared between different vaccination groups using Pearson's chi-squared test and Fisher's exact test, while continuous variables were analyzed using one-way ANOVA test. We used Cox proportional hazards models to estimate the unadjusted and adjusted hazard ratios (aHRs) for acquisition of SARS-CoV-2 infection among participants in different groups of vaccination. Models were adjusted for CD4 count, PVL, different SARS-CoV-2 vaccination and number of mRNA vaccination exposure. A backward stepwise regression with removal threshold of $p = 0.2$ was used to select among covariates to be included into the multivariable model. A two-tailed p value less than 0.05 was considered statistically significant.

The geometric mean titers (GMTs) of SARS-CoV-2 anti-spike IgG were calculated in log-transformed data for statistics. Antibody titers in log form after receiving different vaccines were compared using Student's t-tests at all time-points. Anti-S IgG measurements at each clinic visit were analyzed using generalized estimating equations (GEE) for repeated measurements in the longitudinal follow-up. Logistic regression using the GEE approach was employed to estimate the adjusted odds ratios (aORs) for those with relatively low anti-spike IgG (<1,047, <6,000 or <20,000 BAU/mL) within 16 weeks of vaccination. All analyses were performed using Stata/SE software, Version 17.0 (https://www.stata.com).

## Results

### Participants

Between June 2021 and May 2022, 1556 PWH who were followed at the HIV clinics of NTUH and planned to receive the third dose of COVID-19 vaccine were enrolled. After excluding

those with confirmed SARS-CoV-2 infection, positive anti-N IgG at baseline or during follow-up, and receiving MVC-COV1901 vaccine as the third dose, 1427 PWH who completed the 3-dose vaccination were included for analysis, including 632 (44.3%) who received 100-μg mRNA-1273 vaccine (Group 1), 467 (32.7%) 50-μg mRNA-1273 vaccine (Group 2) and 328 (23.0%) BNT162b2 vaccine (Group 3) (Fig. 1).

Table 1 shows the clinical characteristics of included PWH. The participants were predominantly male (97.6%) with a median age of 40 years; 98.3% were virologically suppressed (defined as having PVL <200 copies/mL) with ART; and their median baseline CD4 count was 631 cells/mm$^3$. Overall, 1377 (96.5%) PLWH were receiving integrase strand-transfer inhibitor-based antiretroviral regimens at enrollment. There were no statistically significant differences in CD4 counts, PVL, and a history of type 2 DM, CKD, malignancies, autoimmune disease, and viral hepatitis among the three groups. The interval between the second and third dose of SARS-CoV-2 vaccination of the participants of Group 1 (median, 79; interquartile range [IQR], 69—92) was shorter than those of Group 2 (106; IQR, 92—143) and 3 (91; IQR, 74—105) ($p < 0.01$).

## Acquisition of new SARS-CoV-2 infection and seroconversion of anti-N IgG

During the 180-day observation, 282 (19.8%) participants were diagnosed as having SARS-CoV-2 infection while the other 92 (6.4%) participants were found to have anti-N IgG seroconversion without obvious COVID-19-associated symptoms. In total, 374 cases of SARS-CoV-2 infection occurred, with 115 (18.2%), 161 (34.5%), and 98 (29.9%) in each group, resulting in an incidence rate of 246.1, 280.8 and 245.2 infections per 1000 person-months of follow-up (Fig. 1). None of the enrolled PWH developed severe or critical COVID-19. There were no statistically significant differences in the infection rates among the three groups (log-rank test for the three groups, $p = 0.28$; Group 2 vs Group 1, $p = 0.10$; Group 3 vs Group 2, $p = 0.63$; and Group 3 vs Group 1, $p = 0.55$) (Fig. 2). In the multivariable Cox regression analysis among all included PWH, independent factors associated with acquisition of SARS-CoV-2 infection were an age older than 50 years (adjusted hazard ratio [aHR], 0.58; 95% CI, 0.43—0.80) and HCV viremia acquired within a year (aHR, 1.33; 95% CI, 1.02—1.72) (Table 2).

## Evolution of anti-S IgG after the third dose of vaccination

Among the participants who received the third dose of SARS-CoV-2 vaccination, anti-S IgG continued to decline regardless of the number of mRNA vaccines and the type of the third vaccine received (Fig. 3). Participants receiving BNT162b2 vaccine as the third dose tended to decline faster than those receiving two different doses of mRNA-1273 vaccine ($p < 0.01$ for data from day 29—56 and

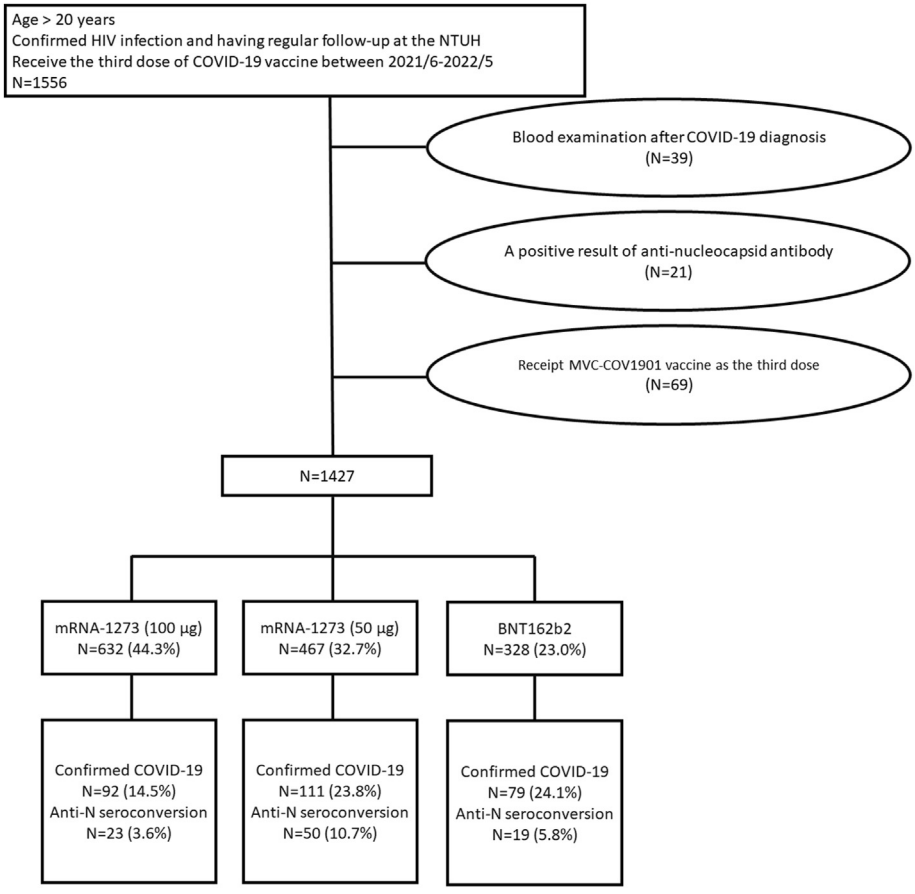


**Figure 1.** Study population.

**Table 1** Baseline characteristics of the included participants. Group 1 represents the participants receiving 100-μg mRNA-1273 vaccine, Group 2 receiving 50-μg mRNA-1273 vaccine and Group 3 receiving BNT162b2 vaccine as the third dose.

| | Total (N = 1427) | Group 1 (N = 632) | Group 2 (N = 467) | Group 3 (N = 328) | p value |
|---|---|---|---|---|---|
| Age (IQR), years | 40 (34–48) | 40 (34–47) | 41 (35–49) | 39 (33–45) | 1.00 |
| Male gender, n (%) | 1395 (97.8) | 622 (98.4) | 459 (98.3) | 314 (95.7) | 0.02 |
| BMI >30 kg/m$^2$, n (%) | 126 (8.8) | 54 (8.5) | 44 (9.4) | 28 (8.5) | 0.86 |
| **HIV status** | | | | | |
| CD4 (IQR), cells/mm$^3$ | 631 (476–813) | 647 (477–806) | 627 (487–833) | 618 (466–800) | 0.95 |
| CD8 (IQR), cells/mm$^3$ | 791 (611–1039) | 787 (604–1066) | 827 (631–1047) | 757 (597–978) | 0.16 |
| CD4 <200 cells/mm$^3$, n (%) | 27 (1.9) | 8 (1.3) | 11 (2.4) | 8 (2.4) | 0.30 |
| CD4 <350 cells/mm$^3$, n (%) | 137 (9.6) | 56 (8.9) | 47 (10.1) | 34 (10.4) | 0.69 |
| CD4 <500 cells/mm$^3$, n (%) | 401 (28.1) | 176 (27.9) | 127 (27.2) | 98 (29.9) | 0.70 |
| Median PVL, (IQR), log copies/mL | 0 (0–0) | 0 (0–0) | 0 (0–0) | 0 (0–0) | 0.37 |
| PVL >20 copies/mL, n (%) | 200 (14.0) | 79 (12.5) | 71 (15.2) | 50 (15.2) | 0.34 |
| PVL >200 copies/mL, n (%) | 24 (1.7) | 7 (1.1) | 12 (2.6) | 5 (1.5) | 0.17 |
| **cART**, n (%) | | | | | |
| INSTI-based | 1377 (96.5) | 609 (96.4) | 456 (97.6) | 312 (95.1) | 0.16 |
| NNRTI-based | 50 (3.5) | 24 (3.8) | 11 (2.4) | 15 (4.6) | 0.21 |
| PI-based | 5 (0.4) | 3 (0.5) | 0 (0) | 2 (0.6) | 0.25 |
| **Comorbidities**, n (%) | | | | | |
| Type 2 DM | 96 (6.7) | 40 (6.4) | 35 (7.5) | 21 (6.4) | 0.72 |
| CKD stage III–V | 78 (5.5) | 33 (5.2) | 30 (6.4) | 15 (4.6) | 0.49 |
| Solid-organ cancer | 32 (2.2) | 14 (2.2) | 13 (2.8) | 5 (1.5) | 0.50 |
| Hematologic malignancy | 28 (2.0) | 11 (1.7) | 11 (2.4) | 6 (1.8) | 0.75 |
| Autoimmune disease | 24 (1.7) | 12 (1.9) | 3 (0.7) | 9 (2.7) | 0.06 |
| Concurrent systemic steroid use | 14 (0.1) | 5 (0.8) | 6 (1.3) | 3 (0.9) | 0.74 |
| Chronic hepatitis B | 157 (11.1) | 67 (10.7) | 52 (11.2) | 38 (11.7) | 0.90 |
| Anti-HCV positivity | 218 (15.4) | 101 (16.1) | 66 (14.3) | 51 (15.6) | 0.69 |
| Receive two mRNA vaccines as the primary vaccination, n (%) | 428 (30.0) | 178 (28.2) | 154 (33.0) | 96 (29.3) | 0.046 |
| Receive no mRNA vaccine as the primary vaccination, n (%) | 935 (65.5) | 433 (68.5) | 284 (60.8) | 218 (66.5) | 0.048 |
| Interval between the second and third dose of SARS-CoV-2 vaccine (IQR), days | 90 (77–109) | 79 (69–92) | 106 (92–143) | 91 (74–105) | <0.001 |

**Abbreviations**: BMI, body-mass index; cART, combination antiretroviral therapy; CKD, chronic kidney disease; DM, diabetes mellitus; HCV, hepatitis C virus; HIV, human immunodeficiency virus; INSTI, integrase strand-transfer inhibitor; IQR, interquartile range; NNRTI, non-nucleoside reverse-transcriptase inhibitor; PI, protease inhibitor; PVL, plasma HIV RNA load.

57–84); however, there were no significant differences of anti-S IgG among the three groups in day 85–112 (data not shown).

Of 1427 PWH who underwent anti-S IgG testing within 16 weeks after receiving the third dose of vaccines, 1005 (70.4%) successfully achieved anti-S IgG titers greater than 1047 BAU/mL, including 460 (72.8%), 342 (73.2%) and 203 (61.9%), respectively, in the three groups. Associated factors with achieving anti-S IgG titers greater than 1047 BAU/mL in the multivariate logistic regression model using GEE included PWH with CD4 counts <200 cells/mm$^3$ before enrollment (adjusted odds ratio [aOR], 0.11; 95% CI, 0.04–0.31), PVL >200 copies/mL (aOR, 0.27; 95% CI, 0.09–0.80), having achieved anti-S IgG >141 BAU/mL within 3 months after primary vaccination (aOR, 3.69, 95% CI, 2.68–5.07), receiving BNT162b2 vaccine as the third dose (aOR, 0.2; 95% CI, 0.10–0.31, Group 1 as reference) and having previously received two doses of mRNA vaccine as primary vaccination (aOR, 2.46; 95% CI, 1.75–3.45, no previous exposure to mRNA vaccine before the third dose as reference) (Table 3). In addition, 260 (18.2%) PWH successfully achieved anti-S IgG titer >6000 BAU/mL, including 108 (17.1%), 102 (21.8%) and 50 (15.2%) in Groups 1, 2, and 3, respectively. Associated factors with achieving anti-S IgG titers >6000 BAU/mL included having achieved anti-S IgG >141 BAU/mL within 3 months after primary vaccination (aOR, 2.74, 95% CI, 1.64–4.57) and having previously received two doses of mRNA vaccine as primary vaccination

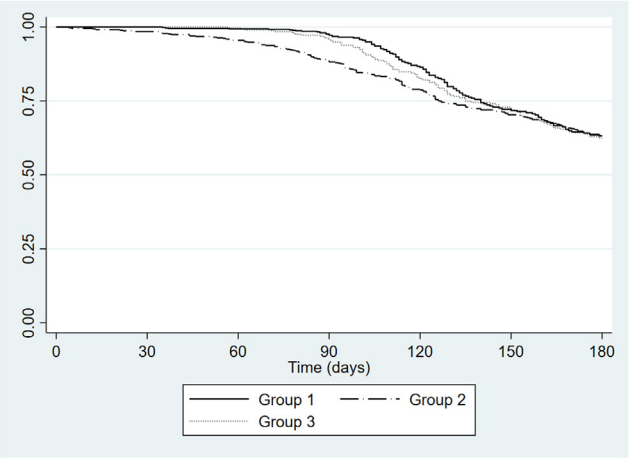


**Figure 2.** Kaplan–Meier survival curve for acquisition of SARS-CoV-2 infection among the three groups. (log-rank test, 3 groups, p = 0.28; log-rank test, Group 2 vs Group 1, p = 0.10; log-rank test, Group 3 vs Group 2, p = 0.63; and log-rank test, Group 3 vs Group 1, p = 0.55).

(aOR, 1.70; 95% CI, 1.19–2.42, no previous exposure to mRNA vaccine before the third dose as reference) (Table 4). Only 56 (8.9%), 56 (12.0%) and 28 (8.5%) PWH of the three groups had an anti-S IgG titer >20,000 BAU/mL. We failed to identify any factors associated with successfully achieving such a high anti-S IgG titer in the statistical model, probably related to small case numbers (data not shown). The anti-S IgG determined 3–6 months after the third dose of vaccination between those who acquired SARS-CoV-2 infection and those who did not were similar, with the GMT of 1732 (95%CI, 1500–2001) and 2005 (95% CI, 1811–2220) BAU/mL (participants with data available, 219 vs 543, p = 0.12) (Supplementary Figure).

## Discussion

In this study investigating the effectiveness and serological responses of the third dose of SARS-CoV-2 vaccination among PWH, we have shown the longitudinal follow-up of acquisition of SARS-CoV-2 infection and antibody responses in PLWH who had been mostly on stable ART with sustained viral suppression and had received different types of the third dose of COVID-19 vaccine in the real-word setting. We have demonstrated similar effectiveness of different vaccine strategies in preventing SARS-CoV-2 infection in PWH regardless the type of the third dose and the 2-dose primary vaccination. Those with a younger age and recently acquired HCV infection were more likely to acquire COVID-19. Moreover, PWH with lower CD4 counts, uncontrolled HIV infection, and who received 50-μg mRNA-1273 and BNT162b2 vaccine as the third dose tended to have suboptimal serological responses.

Until now, evidence on the real-world effectiveness in PWH receiving different third doses of COVID-19 vaccine is scarce. Buchan et al. demonstrated that a third dose was associated with improved vaccine effectiveness against symptomatic infection and severe diseases in general population during the Omicron era.[28] An observation study through analyzing the data from OpenSAFELY platform demonstrated that a marginal benefit of booster vaccination with mRNA-1273 compared with BNT162b2 in preventing SARS-CoV-2 infection and severe disease.[29] A relatively lower prevalence of SARS-CoV-2 infection in Taiwan might contribute to the difference observed when

**Table 2** Factors associated with newly diagnosed SARS-CoV-2 infection and seroconversion of anti-N IgG.

| | Univariable | | Multivariable | |
|---|---|---|---|---|
| | HR (95% CI) | p value | aHR (95% CI) | p value |
| Age >50 years | 0.46 (0.33–0.62) | <0.001 | 0.58 (0.43–0.80) | 0.001 |
| Male gender | 0.84 (0.45–1.58) | 0.59 | – | – |
| BMI >30 kg/m$^2$ | 1.06 (0.74–1.51) | 0.75 | – | – |
| Type 2 DM | 0.71 (0.45–1.13) | 0.15 | – | – |
| CKD stage III–V | 0.86 (0.53–1.41) | 0.56 | – | – |
| Solid-organ cancer | 0.43 (0.14–1.34) | 0.15 | – | – |
| Hematologic malignancy | 1.04 (0.47–2.34) | 0.92 | – | – |
| Autoimmune disease | 0.71 (0.26–1.90) | 0.49 | – | – |
| Concurrent systemic steroid use | 1.52 (0.63–3.68) | 0.35 | – | – |
| Chronic hepatitis B | 0.98 (0.70–1.37) | 0.91 | – | – |
| CD4 <200 cells/mm$^3$ | 0.74 (0.31–1.78) | 0.50 | – | – |
| HCV acquired within a year | 1.40 (1.08–1.82) | 0.01 | 1.33 (1.02–1.72) | 0.03 |
| Syphilis acquired within a year | 1.52 (0.99–2.34) | 0.06 | 1.28 (0.83–1.98) | 0.26 |
| Anti-spike IgG >141 BAU/mL 3 months after the second dose | 1.02 (0.82–1.27) | 0.87 | – | – |
| mRNA-1273 (100-μg) as 3rd dose | Ref | Ref | – | – |
| mRNA-1273 (50-μg) as 3rd dose | 1.21 (0.95–1.54) | 0.12 | – | – |
| BNT162b2 as 3rd dose | 1.15 (0.88–1.51) | 0.30 | – | – |
| mRNA vaccine doses, per 1-dose increase | 0.98 (0.88–1.10) | 0.77 | – | – |

**Abbreviations**: aHR, adjusted hazard ratio; BMI, body-mass index; CKD, chronic kidney disease; DM, diabetes mellitus; HCV, hepatitis C virus; HR, hazard ratio.

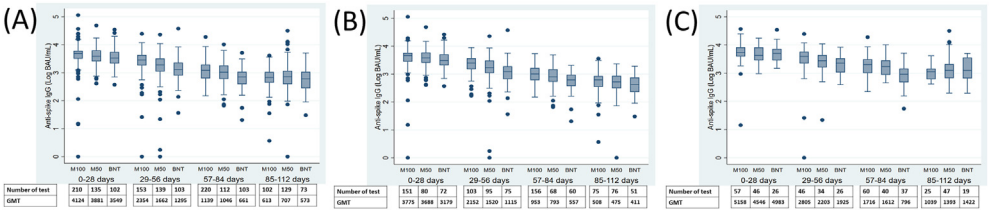


**Figure 3.** Serologic responses after different third dose of COVID-19 vaccination at different follow-up intervals (A) Evolution of anti-spike IgG of all included PWLH. (B). Evolution of anti-spike IgG of PWLH previously receiving no mRNA vaccines. (C) Evolution of anti-spike IgG of PWLH previously receiving two doses of mRNA vaccine. The number in the table below the X-axis in each figure represented the number of PWH undergoing antibody testing and the GMT of anti-spike IgG in each period. Note: M100, mRNA-1273 100-μg; M50, mRNA-1273 50-μg; BNT, BNT162b2.

**Table 3** Factors associated with successfully achieving anti-spike IgG >1047 BAU/mL within 16 weeks.

| | Univariable | | Multivariable | |
|---|---|---|---|---|
| | OR (95% CI) | p value | aOR (95% CI) | p value |
| Age >50 years | 1.11 (0.87–1.41) | 0.41 | – | – |
| Male gender | 0.39 (0.16–0.92) | 0.03 | 0.36 (0.12–1.06) | 0.06 |
| BMI >30 kg/m$^2$ | 1.04 (0.74) | 0.82 | – | – |
| Type 2 DM | 0.91 (0.62–1.32) | 0.61 | – | – |
| CKD stage III–V | 0.99 (0.67–1.48) | 0.97 | – | – |
| Solid-organ cancer | 1.09 (0.59–2.04) | 0.77 | – | – |
| Hematologic malignancy | 1.88 (0.79–4.47) | 0.16 | – | – |
| Autoimmune disease | 1.23 (0.62–2.43) | 0.56 | – | – |
| Concurrent systemic steroid use | 0.62 (0.23–1.63) | 0.33 | – | – |
| Chronic hepatitis B | 0.93 (0.69–1.26) | 0.65 | – | – |
| Chronic hepatitis C | 0.81 (0.62–1.05) | 0.12 | – | – |
| CD4 <200 cells/mm$^3$ | 0.29 (0.14–0.63) | 0.002 | 0.11 (0.04–0.31) | <0.001 |
| CD4 <350 cells/mm$^3$ | 0.75 (0.54–1.04) | 0.09 | – | – |
| CD4 <500 cells/mm$^3$ | 0.84 (0.68–1.03) | 0.09 | – | – |
| PVL >200 copies/mL | 0.44 (0.21–0.95) | 0.04 | 0.27 (0.09–0.80) | 0.02 |
| Anti-spike IgG >141 BAU/mL 3 months after the second dose | 2.73 (2.23–3.35) | <0.001 | 3.69 (2.68–5.07) | <0.001 |
| mRNA-1273 (100-μg) as 3rd dose | Ref | Ref | Ref | Ref |
| mRNA-1273 (50-μg) as 3rd dose | 0.75 (0.60–0.94) | 0.01 | 0.50 (0.25–1.01) | 0.06 |
| BNT162b2 as 3rd dose | 0.51 (0.40–0.65) | <0.001 | 0.20 (0.10–0.41) | <0.001 |
| Previously no mRNA vaccine exposure | Ref | Ref | Ref | Ref |
| Previously receiving one dose of mRNA vaccine | 1.92 (1.09–3.38) | 0.02 | 2.33 (1.08–5.05) | 0.03 |
| Previously receiving two doses of mRNA vaccine | 2.39 (1.90–3.01) | <0.001 | 2.46 (1.75–3.45) | <0.001 |

**Abbreviations**: aOR, adjusted odds ratio; BMI, body-mass index; CKD, chronic kidney disease; DM, diabetes mellitus; HCV, hepatitis C virus; OR, odds ratio; PVL, plasma HIV RNA load.

our study was conducted. Our study also echoed the study by Nguyen et al., which revealed that, among mRNA-boosted adults, those who underwent a non-mRNA primary vaccination and mRNA booster vaccination experienced a similar rate of SARS-CoV-2 infection compared with those who received BNT162b2 in primary vaccination.[30] Nevertheless, the titer of anti-S IgG was higher in our participants who had received mRNA vaccines in primary vaccination, though the durability of vaccine effectiveness warrants further investigation.

Previous studies have shown that the factors associated with breakthrough SARS-CoV-2 infection among immunocompromised patients include older age, multiple comorbidities and suboptimal antibody response after primary vaccination.[10,26,28,31] However, such factors were not found in our study. On the contrary, we found that people aged <50 years and those with recently acquired HCV infection were more likely to become infected with SARS-CoV-2 during the follow-up. The explanation for this finding remains speculative that PWH might be less likely to keep practicing physical distancing, as shown in a cross-sectional study conducted in Nigeria.[32] Moreover, recently acquired HCV infection among PWH with male-to-male sex had risky sexual contacts, which might explain the association of recently acquired HCV infection with a higher SARS-CoV-2 infection rate in our cohort.[33,34]

To date, several studies have demonstrated that PWH on stable ART have considerable antibody responses after the booster vaccination compared with HIV-negative controls.[35] In a retrospective study of 84 PWH with CD4 count

**Table 4** Factors associated with successfully achieving anti-spike IgG >6000 BAU/mL within 16 weeks.

| | Univariable | | Multivariable | |
|---|---|---|---|---|
| | OR (95% CI) | p value | aOR (95% CI) | p value |
| CD4 <200 cells/mm$^3$ | 0.38 (0.05–2.81) | 0.34 | – | – |
| PVL >200 copies/mL | 0.46 (0.07–3.12) | 0.42 | – | – |
| Anti-spike IgG >141 BAU/mL 3 months after the second dose | 3.22 (1.97–5.27) | <0.001 | 2.74 (1.64–4.57) | <0.001 |
| mRNA-1273 (100-μg) as 3rd dose | Ref | Ref | – | – |
| mRNA-1273 (50-μg) as 3rd dose | 1.07 (0.74–1.56) | 0.71 | – | – |
| BNT162b2 as 3rd dose | 0.71 (0.45–1.12) | 0.14 | – | – |
| Previously no mRNA vaccine exposure | Ref | Ref | Ref | Ref |
| Previously receiving one dose of mRNA vaccine | 0.22 (0.03–1.65) | 0.14 | 0.17 (0.02–1.24) | 0.08 |
| Previously receiving two doses of mRNA vaccine | 2.23 (1.59–3.13) | <0.001 | 1.70 (1.19–2.42) | 0.003 |

**Abbreviations**: aOR, adjusted odds ratio; OR, odds ratio; PVL, plasma HIV RNA load.

>500 cells/mm$^3$, anti-S IgG increased significantly after mRNA-1273 or BNT162b2 booster vaccination; however, current CD4 status and receipt of mRNA vaccine were not found to be associated with the serological responses.[36] In our study, PWH with CD4 <200 cells/mm$^3$ remained an associated factor with suboptimal antibody responses, similar to what we had observed in PWH having received two homologous primary vaccines.[11] For PWH who had a lower antibody response after primary vaccination, Jongkees et al. demonstrated a successful restoration of serological response to an additional third dose with 100-μg mRNA-1273 vaccine.[37] Our study yielded similar results and further indicated that a third dose with 100-μg mRNA-1273 vaccine led to a higher antibody response compared with 50-μg mRNA-1273 and BNT162B2 vaccine.

We demonstrated in this study that those receiving a BNT162b2 vaccine as the third dose tended to have a suboptimal anti-S IgG response; however, the vaccine effectiveness against acquiring SARS-Cov-2 infection was similar between those who received the 100-ug and those who received 50-ug mRNA-1273 vaccine. Such discordance might be attributed to a relatively small case number or less severe epidemic in Taiwan when the study was conducted, which could preclude the precise estimation of vaccine effectiveness. In addition, the protective mechanism of the COVID-19 vaccination could be more than just IgG response. First, vaccination can elicit a mucosal immune response and secretory IgA is the main functional indicator. However, the correlation between mucosal IgA and systemic IgG induced by currently available vaccines is unclear. Second, long-lasting T-cell memory can facilitate a response in people infected with SARS-CoV-2. Compared with other variants of concern, suboptimal responses were found against the Omicron variant despite the type of vaccination. CD4 T cells of PWH may be less effective to activate B cells to generate neutralization antibodies.[38]

In this study, we failed to correlate the titers of anti-S IgG with acquisition of SARS-CoV-2. The IgG data before those who acquired SARS-CoV-2 infection was similar to the control group whom did not acquire COVID-19 in the same time frame. Despite bias caused by multiple comparisons, such findings echoed those of the study by Dimeglio C, et al., in which extremely high anti-S titers following vaccination still failed to confer adequate protection against the Omicron variant.[27]

The strengths of this study include a large number of PWH and a longer observational period for the evaluation of antibody responses even before the third dose. However, there are several limitations in this study. First, the rate of asymptomatic infection could have been underestimated by simply testing for anti-N IgG. Anti-N IgG might wane one year after primary SARS-CoV-2 infection.[39] In addition, Socan et al. demonstrated that seropositive rate of anti-N IgG in people with SARS-CoV-2 infection was lower in vaccinated people than those without previous vaccination.[40] On the other hand, anti-N IgG antibodies were found to share cross-reactivity between SARS-CoV-2, SARS-CoV, and seasonal coronaviruses, which makes the estimation of asymptomatic SARS-CoV-2 infection difficult.[41] Second, we did not include PWH who only underwent primary vaccination for comparison, and therefore, the benefit of the third dose of vaccination in preventing breakthrough infections could not be evaluated in our study. Third, not all of the anti-S IgG measurements were performed at fixed time-points. The evolution of serological responses should be interpreted with caution despite the similar trends to those observed in other studies.[6] Fourth, we did not obtain the history of anti-SARS-CoV-2 medications and none of the participants developed severe disease with oxygen desaturation; vaccine effectiveness against severe infection might be overestimated. Fifth, no HIV-negative participants were included as a control group, which might preclude us from understanding if vaccine effectiveness or serological responses to COVID-19 vaccination among virally-suppressed PWH were similar to that among people without HIV infection. Sixth, this study was conducted during the community outbreak of Omicron subvariant BA.2 in Taiwan. The vaccine effectiveness could not be generalized in the era of subsequent circulating subvariant including BA.4 or BA.5. Sixth, we only included those receiving mRNA vaccines as the third dose and excluded those receiving protein-based vaccination including MVC-COV1901 and NVX-CoV2373 vaccines. Last, we did not assess the neutralizing antibody or T cell-related immunity. Instead, several cut-off values derived from an immune-bridging model were used in our study. Nevertheless, the

performance of using the immune-bridging model to predict vaccine effectiveness against SARS-CoV-2 infection or severe infection in the era of Omicron variant warrants more investigations among PWH.

In conclusion, we found PWH receiving different types of the third dose of mRNA COVID-19 vaccine showed similar effectiveness against SARS-CoV-2 infection. Acquisition of COVID-19 was associated with a younger age and recent HCV infection. An additional dose with 100-μg mRNA-1273 could generate a higher antibody response than 50-μg mRNA-1273 and BNT162b2 vaccine, which might confer benefit in terms of antibody titers in those with suboptimal serological responses after primary vaccination. CD4 counts less than 200 cells/mm$^3$ and PVL greater than 200 copies/mL still contributed to lower anti-S IgG titers.

## Funding

This work was supported by Taiwan National Science and Technology Council (grant # NSTC 112-2321-B-002-013 and 111-2314-B-002-302).

## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## Acknowledgements

We would like to thank all of the participants who participated in this longitudinal follow-up study. The preliminary data of the present study have been presented in a poster presentation form (abstract no. 1020) in Conference on Retroviruses and Opportunistic Infections (CROI) 2023, Seattle, US, 19—22, February, 2023.

## References

1. Wu PY, Sun HY, Sheng WH, Hsieh SM, Chuang YC, Huang YS, et al. Impact of coronavirus disease 2019 on the HIV testing and health care delivery at a university hospital in Taiwan, 2020—2021. *J Microbiol Immunol Infect* 2022;**55**:1005—12.
2. Liu WD, Wang HY, Du SC, Hung CC. Impact of the initial wave of COVID-19 pandemic in Taiwan on local HIV services: results from a cross-sectional online survey. *J Microbiol Immunol Infect* 2022;**55**:1135—43.
3. Lin KY, Wu PY, Liu WD, Sun HY, Hsieh SM, Sheng WH, et al. Effectiveness of COVID-19 vaccination among people living with HIV during a COVID-19 outbreak. *J Microbiol Immunol Infect* 2022;**55**:535—9.
4. Frater J, Ewer KJ, Ogbe A, Pace M, Adele S, Adland E, et al. Safety and immunogenicity of the ChAdOx1 nCoV-19 (AZD1222) vaccine against SARS-CoV-2 in HIV infection: a single-arm substudy of a phase 2/3 clinical trial. *Lancet HIV* 2021;**8**:e474—85.
5. Madhi SA, Moodley D, Hanley S, Archary M, Hoosain Z, Lalloo U, et al. Immunogenicity and safety of a SARS-CoV-2 recombinant spike protein nanoparticle vaccine in people living with and without HIV-1 infection: a randomised, controlled, phase 2A/2B trial. *Lancet HIV* 2022;**9**:e309—22.
6. Jedicke N, Stankov MV, Cossmann A, Dopfer-Jablonka A, Knuth C, Ahrenstorf G, et al. Humoral immune response following prime and boost BNT162b2 vaccination in people living with HIV on antiretroviral therapy. *HIV Med* 2022;**23**:558—63.
7. Chambers C, Samji H, Cooper CL, Costiniuk CT, Janjua NZ, Kroch AE, et al. Coronavirus disease 2019 vaccine effectiveness among a population-based cohort of people living with HIV. *AIDS* 2022;**36**:F17—26.
8. Fowokan A, Samji H, Puyat JH, Janjua NZ, Wilton J, Wong J, et al. Effectiveness of COVID-19 vaccines in people living with HIV in British Columbia and comparisons with a matched HIV-negative cohort: a test-negative design. *Int J Infect Dis* 2023;**127**:162—70.
9. Tuan JJ, Zapata H, Barakat L, Andrews L, Behnegar A, Kim YW, et al. Long-term quantitative assessment of anti-SARS-CoV-2 spike protein immunogenicity (QUASI) after COVID-19 vaccination in older people living with HIV (PWH). *BMC Infect Dis* 2022;**22**:744.
10. Lang R, Humes E, Coburn SB, Horberg MA, Fathi LF, Watson E, et al. Analysis of severe illness after postvaccination COVID-19 breakthrough among adults with and without HIV in the US. *JAMA Netw Open* 2022;**5**:e2236397.
11. Liu WD, Pang MW, Wang JT, Sun HY, Huang YS, Lin KY, et al. Evolution of anti-SARS-CoV-2 spike protein titers after two-dose of COVID-19 vaccination among people living with HIV. *J Virus Erad* 2022;**8**:100308.
12. Rössler A, Riepler L, Bante D, von Laer D, Kimpel J. SARS-CoV-2 Omicron variant neutralization in serum from vaccinated and convalescent persons. *N Engl J Med* 2022;**386**:698—700.
13. Department of Health and Human Services, National Institutes of Health. *Guidance for COVID-19 and people with HIV* [Internet]. 2021 [cited 2022 Nov 2]. Available from: https://clinicalinfo.hiv.gov/en/guidelines/guidance-covid-19-and-people-hiv/guidance-covid-19-and-people-hiv.
14. Baden LR, El Sahly HM, Essink B, Kotloff K, Frey S, Novak R, et al. Efficacy and safety of the mRNA-1273 SARS-CoV-2 vaccine. *N Engl J Med* 2021;**384**:403—16.
15. Polack FP, Thomas SJ, Kitchin N, Absalon J, Gurtman A, Lockhart S, et al. Safety and efficacy of the BNT162b2 mRNA COVID-19 vaccine. *N Engl J Med* 2020;**383**:2603—15.
16. The U.S Centers for Disease Control. *HIV and COVID-19 basics* [Internet]. 2023 [cited 2023 Mar 13]. Available from: https://www.cdc.gov/hiv/basics/covid-19.html.
17. Chen YH, Fang CT. Combined interventions to suppress R0 and border quarantine to contain COVID-19 in Taiwan. *J Formos Med Assoc* 2021;**120**:903—5.
18. Chen SC. Taiwan's experience in fighting COVID-19. *Nat Immunol* 2021;**22**:393—4.
19. Press Releases [Internet] *Taiwan centers for disease control*. 2021 [cited 2022 Nov 2]. Available from: https://www.cdc.gov.tw/Category/ListContent/EmXemht4IT-IRAPrAnyG9A?uaid=m00G4Iadc5c7bts6_BIahw.
20. Hsieh SM, Liu MC, Chen YH, Lee WS, Hwang SJ, Cheng SH, et al. Safety and immunogenicity of CpG 1018 and aluminium hydroxide-adjuvanted SARS-CoV-2 S-2P protein vaccine MVC-COV1901: interim results of a large-scale, double-blind, randomised, placebo-controlled phase 2 trial in Taiwan. *Lancet Respir Med* 2021;**9**:1396—406.
21. Cheng SH, Lien CE, Hsieh SM, Cheng CY, Liu WD, Lo CL, et al. A retrospective study of the safety and immunogenicity of MVC-COV1901 vaccine for people living with HIV. *Vaccines* 2022;**11**:18.
22. Press Releases [Internet] *Taiwan centers for disease control*. 2021 [cited 2022 Nov 2]. Available from: https://www.cdc.gov.tw/Category/ListContent/HN_bvfRk6F9P3-V-G4NJxQ?uaid=jFA9aSRe4fJ1WucCcr94BA.
23. World Health Organization. *Interim recommendations for an extended primary series with an additional vaccine dose for COVID-19 vaccination in immunocompromised persons*

[Internet]. 2021 [cited 2023 Mar 13]. Available from: https://www.who.int/publications/i/item/WHO-2019-nCoV-vaccines-SAGE_recommendation-immunocompromised-persons.
24. Liu WD, Wang JT, Chao TL, Ieong SM, Tsai YM, Kuo PH, et al. Evolution of neutralizing antibodies and cross-activity against different variants of SARS-CoV-2 in patients recovering from COVID-19. *J Formos Med Assoc* 2023;**122**:714—22.
25. Dimeglio C, Herin F, Martin-Blondel G, Miedougé M, Izopet J. Antibody titers and protection against a SARS-CoV-2 infection. *J Infect* 2022;**84**:248—88.
26. Stærke NB, Reekie J, Nielsen H, Benfield T, Wiese L, Knudsen LS, et al. Levels of SARS-CoV-2 antibodies among fully vaccinated individuals with Delta or Omicron variant breakthrough infections. *Nat Commun* 2022;**13**:4466.
27. Dimeglio C, Migueres M, Bouzid N, Chapuy-Regaud S, Gernigon C, Da-Silva I, et al. Antibody titers and protection against Omicron (BA.1 and BA.2) SARS-CoV-2 infection. *Vaccines* 2022;**10**:1548.
28. Buchan SA, Chung H, Brown KA, Austin PC, Fell DB, Gubbay JB, et al. Estimated Effectiveness of COVID-19 vaccines against Omicron or Delta symptomatic infection and severe outcomes. *JAMA Netw Open* 2022;**5**:e2232760.
29. Hulme WJ, Horne EMF, Parker EPK, Keogh RH, Williamson EJ, Walker V, et al. Comparative effectiveness of BNT162b2 versus mRNA-1273 covid-19 vaccine boosting in England: matched cohort study in OpenSAFELY-TPP. *BMJ* 2023;**380**:e072808.
30. Nguyen VG, Yavlinsky A, Beale S, Hoskins S, Byrne TE, Lampos V, et al. Comparative effectiveness of different primary vaccination courses on mRNA-based booster vaccines against SARs-COV-2 infections: a time-varying cohort analysis using trial emulation in the Virus Watch community cohort. *Int J Epidemiol* 2023;**52**:342—54.
31. Herting A, Jahnke-Triankowski J, Harberts A, Schaub GM, Lütgehetmann M, Ruether DF, et al. Clinical outcomes of SARS-CoV-2 breakthrough infections in liver transplant recipients during the Omicron wave. *Viruses* 2023;**15**:297.
32. Folayan MO, Ibigbami O, Brown B, El Tantawi M, Uzochukwu B, Ezechi OC, et al. Differences in COVID-19 preventive behavior and food insecurity by HIV status in Nigeria. *AIDS Behav* 2022;**26**:739—51.
33. Chen GJ, Sun HY, Chang SY, Su LH, Chen YT, Hsieh SM, et al. Sexually-transmitted hepatitis C virus reinfections among people living with HIV in Taiwan: the emerging role of genotype 6. *Emerg Microb Infect* 2022;**11**:1227—35.
34. Huang MH, Chen GJ, Sun HY, Chen YT, Su LH, Ho SY, et al. Risky sexual practices and hepatitis C viremia among HIV-positive men who have sex with men in Taiwan. *J Microbiol Immunol Infect* 2023;**56**:566—74.
35. Lapointe HR, Mwimanzi F, Cheung PK, Sang Y, Yaseen F, Umviligihozo G, et al. People with HIV receiving suppressive antiretroviral therapy show typical antibody durability after dual COVID-19 vaccination, and strong third dose responses. *J Infect Dis* 2023;**227**:838—49.
36. Malin JJ, Suárez I, Biehl LM, Schommers P, Knops E, Di Cristanziano V, et al. Immune response to mRNA-based COVID-19 booster vaccination in people living with HIV. *HIV Med* 2023;**24**:785—93.
37. Jongkees MJ, Geers D, Hensley KS, Huisman W, GeurtsvanKessel CH, Bogers S, et al. Immunogenicity of an additional mRNA-1273 SARS-CoV-2 vaccination in people with HIV with hyporesponse after primary vaccination. *J Infect Dis* 2023;**227**:651—62.
38. Yang H, Xie Y, Li C. Understanding the mechanisms for COVID-19 vaccine's protection against infection and severe disease. *Expert Rev Vaccines* 2023;**22**:186—92.
39. Van Elslande J, Oyaert M, Lorent N, Vande Weygaerde Y, Van Pottelbergh G, Godderis L, et al. Lower persistence of anti-nucleocapsid compared to anti-spike antibodies up to one year after SARS-CoV-2 infection. *Diagn Microbiol Infect Dis* 2022;**103**:115659.
40. Socan M, Prosenc K, Mrzel M. Seroprevalence of anti-SARS-CoV-2 antibodies following the Omicron BA.1 wave. *Int J Environ Res Publ Health* 2023;**20**:3665.
41. Galipeau Y, Siragam V, Laroche G, Marion E, Greig M, McGuinty M, et al. Relative ratios of human seasonal coronavirus antibodies predict the efficiency of cross-neutralization of SARS-CoV-2 spike binding to ACE2. *EBioMedicine* 2021;**74**:103700.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jmii.2024.02.004.