



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



ELSEVIER

Contents lists available at ScienceDirect

## International Journal of Infectious Diseases

journal homepage: [www.elsevier.com/locate/ijid](http://www.elsevier.com/locate/ijid)

## Review

## Immunogenicity and efficacy of COVID-19 vaccines in people living with HIV: a systematic review and meta-analysis

Juntao Yin<sup>1</sup>, Yangyang Chen<sup>2</sup>, Yang Li<sup>1</sup>, Chaoyang Wang<sup>3,\*,\*</sup>, Xingwang Zhang<sup>4,\*,\*</sup><sup>1</sup> Department of Pharmacy, Huaihe Hospital, Henan University, Henan, China<sup>2</sup> Cardiology, Huaihe Hospital, Henan University, Henan, China<sup>3</sup> Institute of Evidence-based Medicine and Translational Medicine, Department of Medicine, Henan University, Henan, China<sup>4</sup> Department of Pharmaceutics, School of Pharmacy, Jinan University, Guangdong, China

## ARTICLE INFO

## Article history:

Received 31 August 2022

Revised 30 September 2022

Accepted 3 October 2022

## Keywords:

COVID-19

HIV

Immunogenicity

SARS-CoV-2

Vaccination

Meta-analysis

## ABSTRACT

**Objectives:** Available data show that COVID-19 vaccines may be less effective in people living with HIV (PLWH) who are at increased risk for severe COVID-19. This meta-analysis aimed to compare the immunogenicity and efficacy of COVID-19 vaccines in PLWH with healthy individuals.

**Methods:** Pubmed/Medline, EMBASE, and the Cochrane Library were searched. Risk ratios of seroconversion were separately pooled using random-effects meta-analysis, and a systematic review without meta-analysis of SARS-CoV-2 antibody titer levels was performed after the first and second doses of a COVID-19 vaccine.

**Results:** A total of 22 studies with 6522 subjects met the inclusion criteria. After the first vaccine dose, seroconversion in PLWH was comparable to that in healthy individuals. After a second dose, seroconversion was slightly lower in PLWH compared with healthy controls, and antibody titers did not seem to be significantly affected or reduced among participants of both groups.

**Conclusion:** COVID-19 vaccines show favorable immunogenicity and efficacy in PLWH. A second dose is associated with consistently improved seroconversion, although it is slightly lower in PLWH than in healthy individuals. Additional strategies, such as a booster vaccination with messenger RNA COVID-19 vaccines, might improve seroprotection for these patients.

© 2022 The Author(s). Published by Elsevier Ltd on behalf of International Society for Infectious Diseases.

This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>)

## Introduction

The transmission of SARS-CoV-2 has led to the ongoing global COVID-19 pandemic. By August 19, 2022, more than 590 million have had confirmed COVID-19 and more than 6 million have died worldwide (World Health Organization, 2022). The morbidity and mortality from COVID-19 and its complications and large-scale economic disruption have prompted an unprecedented pace in highly efficacious vaccine development (Berlin *et al.*, 2020; Merad *et al.*, 2022). As of August 19, 2022, a total of 12.4 billion vaccine doses have been administered (World Health Organization, 2022), and the most widely used are messenger RNA (mRNA) vaccines, includ-

ing BNT162b2 (Pfizer-BioNTech, New York, NY, USA-Mainz, Germany) and mRNA-1273 (Moderna, Cambridge, MA, USA) vaccines and viral vector vaccines, such as Ad26.CoV2.S (Johnson & Johnson, New Brunswick, NJ, USA), ChAdOx (AstraZeneca, Cambridge, UK), Sputnik V (Gamaleya Research Institute of Epidemiology and Microbiology, Moscow, Russia), and the traditional inactivated virus alum-adsjuvanted candidate vaccine CoronaVac (Sinovac, Beijing, China) (Piccaluga *et al.*, 2022). All of these vaccines were well tolerated in clinical trials, and their proven efficacy was higher than 90% in preventing symptomatic laboratory-confirmed SARS-CoV-2 infection, except for the CoronaVac vaccine, which only had proven effectiveness of 51% (Baden *et al.*, 2021; Kyriakidis *et al.*, 2021; Mallapaty, 2021; Vergnes, 2021). High seroconversion rates were shown regardless of the class of vaccine used or previous infection status (Eyre *et al.*, 2021).

Vaccine trials, however, did not report data about people living with HIV (PLWH) groups separately, leading to a paucity of data on the efficacy and safety of vaccines in the PLWH groups.

\* Corresponding authors.

E-mail addresses: [yinjuntao811@163.com](mailto:yinjuntao811@163.com) (J. Yin), [45954356@qq.com](mailto:45954356@qq.com) (Y. Chen), [hnszyy0502@163.com](mailto:hnszyy0502@163.com) (Y. Li), [hyt0378@163.com](mailto:hyt0378@163.com) (C. Wang), [zhangxw@jnu.edu.cn](mailto:zhangxw@jnu.edu.cn) (X. Zhang).

# These authors contributed equally to this work.

These patients, who comprise only a small minority of the global population, are of particular interest because of possible suppression or overactivation of the immune system attributable to the primary disease or concurrent treatment (Lee et al., 2022). Data are urgently needed on PLWH because infection and viral shedding have been reported to be more severe and persistent in this group (Cederwall and Pählman, 2020; Couch et al., 1997; Manuel and Estabrook, 2019). PLWH are at increased risk for COVID-19-related complications and death (Silveira et al., 2021; Ssentongo et al., 2021).

Studies have shown variable efficacy of other vaccines, such as influenza and hepatitis B virus (HBV) vaccines, which is thought to depend on factors such as vaccine type and concurrent drugs, in the PLWH groups. In a meta-analysis on the immunogenicity of influenza vaccination in PLWH, trivalent inactivated influenza vaccines are effective in preventing influenza infection in PLWH (Remschmidt et al., 2014). In another meta-analysis, a double dose of the HBV vaccine and multiple injections were associated with better immune responses than the standard HBV vaccine regimen in PLWH, and higher seroconversion rates were observed in PLWH with high clusters of differentiation (CD 4+) T-cell levels, suggesting that PLWH should receive HBV vaccine as soon as possible after HIV diagnosis (Tian et al., 2021). HIV is characterized by attenuated humoral immunity that may reduce the efficacy of vaccines in PLWH, and there are major gaps in knowledge on the efficacy of COVID-19 vaccines in PLWH, especially in the context of all the knowledge about the efficacy of other vaccines in this population (Oyelade et al., 2022).

There are some meta-analyses now in a preprint on the immunogenicity of COVID-19 vaccines in PLWH cohorts, but a systematic exploration of related factors is still lacking. In this meta-analysis, we compared seroconversion rates and antibody titer levels for different COVID-19 vaccines between PLWH and healthy controls.

## Methods

This systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines (Page et al., 2021), and a review protocol (CRD42022356167) with search strategy was registered in the International Prospective Register of Systematic Reviews.

### Search strategy

A comprehensive electronic search (from December 1, 2020 to August 10, 2022) of PubMed/Medline, EMBASE, and the Cochrane Library was conducted for articles published. No language restrictions were imposed. To improve the validity of data, we excluded nonpeer-reviewed articles in preprint databases. The reference lists of all included articles were also hand searched to identify any potentially eligible studies.

We used a two-stage approach for screening: first, by title and abstract and then, by full-text article. Two researchers (JY and CW) independently screened each title, abstract, and full text. Data were crosschecked, and any discrepancies were resolved by discussion or consultation with a third independent investigator (XS). Studies were limited to human participants and of any follow-up duration and time points.

### Inclusion and exclusion criteria

We performed a meta-analysis of prospective studies that met the following criteria: included human participants who received a COVID-19 vaccine of any brand and type, people living with HIV/AIDS, studies that included and reported data on a control

group comprising individuals who are not infected with HIV, and studies that reported at least one seroconversion after COVID-19 vaccination or serological titers after COVID-19 vaccination.

We excluded studies that enrolled but did not report outcomes of a control group; reported seroconversion data in a form that prevented the calculation of proportions, risk of seroconversion, or the number of seroconverted participants; and reported serological titers in a form from which neither mean nor median titers could be derived.

When studies did not provide available data, we contacted the corresponding authors through email for information. We excluded studies only if data were not provided at the time of meta-analysis.

In light of the emergence of clinical studies on a third dose of COVID-19 vaccine in PLWH, we made a *post hoc* amendment to include studies reporting these data for qualitative analysis, prospective observational or experimental studies that involved human participants, all of whom should be receiving a COVID-19 vaccine of any brand and type, studies that involved people living with HIV/AIDS, and studies that reported seroconversion rates of PLWH with or without the inclusion of a control group.

### Data extraction

Two researchers (JY and CW) synthesized data from all eligible studies and created graphs using a Microsoft Excel spreadsheet. At the end of the data extraction phase, all key extracted data were reviewed and quality checked by the same two researchers.

Data on study characteristics comprised setting, primary and secondary outcomes, study design, sample size, dropout and non-response rates, and inclusion and exclusion criteria. Participant data comprised age, sex, and disease and treatment history, including immunosuppressive regimen. Intervention-related data included vaccine type and brand, dosing schedule, number of participants receiving each type and brand of vaccine, and median or mean interval between doses. Outcome-related data comprised assay type, antibody measured, method of measurement, intervals of sample collection, and number of measurements.

### Quality assessment

The risk of bias in nonrandomized studies of interventions tool was used to rate the risk of bias for nonrandomized included studies. This tool assesses seven domains: risk of bias from confounding, selection of participants, classification of interventions, deviations from intended interventions, missing data, measurement of outcomes, and selection of the reported results (Lee et al., 2022). Two investigators (JY and CW) independently judged these domains as low, moderate, serious, or critical risk of bias or no information. All discrepancies were first discussed between the investigators, then split by a third investigator (XZ) in case of persistent discordance. A study would be judged as having an overall low risk of bias if all the domains were judged as low risk. A study would be considered as having critical risk of bias if one domain was judged to be at high risk of bias. Assessment for publication bias was qualitative, through visual inspection for funnel plot asymmetry (Egger et al., 1997).

A standardized method, namely, version 2 of the Cochrane risk of bias tool was used for randomized trials (Sterne et al., 2019). During this study, however, no eligible randomized studies were found.

### Data analysis

The primary outcomes of interest were seroconversion after a first and second dose of the COVID-19 vaccine. As brand and type

of assay, type of immunoglobulin (Ig), and definition of seroconversion differed across studies, Table 1 reports the respective data for each included study.

As the type of antibodies measured and reported differed across studies, Supplementary Tables 1 and 2 show the titers after a first and second vaccine dose, respectively. The time points of serological assessment after COVID-19 vaccination and the different brands of serological kits are shown in Table 1. We used a random-effects model to estimate the pooled risk ratios (RRs) and corresponding 95% confidence intervals (CIs) for the primary outcomes of interest. An RR < 1 indicates that PLWH had a lower risk of achieving seroconversion after COVID-19 vaccination than the control groups. Statistical heterogeneity of the results in the enrolled studies was assessed by the chi-squared test and  $I^2$  statistic. We considered heterogeneity to be significant when the  $P$ -value < 0.05 or the  $I^2$  statistic was  $\geq 50\%$  (Higgins and Thompson, 2002).

We performed subgroup analyses to determine if the results were influenced by the types of COVID-19 vaccine.

Because the SARS-CoV-2 antibody titer levels cannot be amenable to statistical pooling due to different methods and assays used, secondary outcomes were assessed using the synthesis review without a meta-analysis approach.

We performed separate meta-analyses for the RR of seroconversion (measured as RR compared with healthy controls) after each vaccine dose. Mixed-effects models were used to pool the logit transformed proportions of PLWH who achieved seroconversion after a first and second COVID-19 vaccine dose.

Statistical analyses were performed using RevMan 5.4 (Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2020). The certainty of the evidence was assessed using the Grading of Recommendations Assessment, Development, and Evaluation (Guyatt et al., 2008).

## Results

### Study selection and characteristics

The selection procedure is summarized in Figure 1. Overall, 22 studies were included in the meta-analysis of seroconversion rates (Table 1) (Antinori et al., 2022; Bergman et al., 2021; Brumme et al., 2022; Feng et al., 2022; Frater et al., 2021; Heftdal et al., 2022; Huang et al., 2022; Jedicke et al., 2022; Khan et al., 2021; Levy et al., 2021; Lombardi et al., 2022; Lv et al., 2022; Madhi et al., 2021; Madhi et al., 2022; Netto et al., 2022; Ogbe et al., 2022; Rahav et al., 2021; Schmidt et al., 2022; Tuan et al., 2022; Woldemeskel et al., 2021; Zeng et al., 2022; Zou et al., 2022). Tables S1 and S2 present the serological antibody titers after a first and second dose of COVID-19 vaccines, respectively. In addition, one study that met the inclusion criteria for the meta-analysis was excluded because seroconversion rates among healthy controls could not be obtained in time from the corresponding authors (González de Aledo et al., 2022).

Of the 22 included studies, 10 (45%) used mRNA vaccines BNT162b2 (Pfizer-BioNTech) and mRNA-1273 (Moderna), six (27%) inactivated vaccines CoronaVac (Sinovac, Biotech) and BBIBP-CorV (SinoPharm-Beijing BBIBP-CorV), five (23%) studies involving viral vector vaccines AZD1222 (ChAdOx1 nCoV-19; Oxford-AstraZeneca) and Ad26.CoV2.S (Janssen/Johnson & Johnson), and one (5%) recombinant spike protein nanoparticle vaccine co-formulated with a saponin-based adjuvant Matrix-M (NVX-CoV2373; Novavax; Gaithersburg, MD, USA). In one study, BNT162b2, mRNA-1273, and AZD1222 were used simultaneously (Brumme et al., 2022). Among the viral vector vaccines, AZD1222 was used in four (18%) studies (Brumme et al., 2022; Frater et al., 2021; Madhi et al., 2021; Ogbe et al., 2022) and as the sole vaccine in three (14%) (Frater et al., 2021; Madhi et al., 2021; Ogbe et al., 2022), and Ad26.CO2.S was

used in only one (5%) study (Khan et al., 2021). Therefore, AZD1222 featured more prominently.

### Vaccine response

Seven studies reported seroconversion after a first vaccine dose in PLWH ( $n = 603$ ) compared with healthy controls ( $n = 884$ ). There was no difference in the seroconversion rate between PLWH and healthy controls (RR 0.95, 95% CI 0.89–1.03,  $I^2 = 86\%$ , Figure 2) (moderate certainty of the evidence).

In 20 studies with a total of 2068 PLWH and 4454 healthy controls, seroconversion rates were lower among the PLWH than the healthy controls after a second vaccine dose (RR 0.92, 95% CI 0.87–0.97,  $I^2 = 92\%$ , Figure 3) (moderate certainty of the evidence).

Antibody titers did not seem to be significantly affected or reduced among participants after a second vaccine dose, with Lombardi et al. (2022) reporting a 0.44-fold reduction among eight healthy controls (median 1077 U/ml, interquartile range [IQR] 702–7551 U/ml) compared with 62 PLWH (median 2437 U/ml, IQR 1485–4526 U/ml) and Netto et al. (2022) reporting a 0.64-fold reduction among 204 PLWH (median 48.7 AU/ml, IQR 26.6–88.2 AU/ml) compared with 274 controls (median 75.2 AU/ml, IQR 50.3–112.0 AU/ml).

### Heterogeneity in PLWH after the first and second doses

A subgroup analysis was performed for studies involving only mRNA vaccines and only non-mRNA vaccines after the first and second doses. After the first dose, there were no significant differences ( $P$ -value = 0.92 for test of subgroup effect; Figure 4) in the effects on seroconversion between mRNA vaccines (RR 0.87, 95% CI 0.60–1.27) and non-mRNA vaccines (RR 0.85, 95% CI 0.66–1.11). After the second dose, no significant differences ( $P$ -value = 0.03 for test of subgroup effect, Figure 5) were found in the effects on seroconversion between mRNA vaccines (RR 0.96, 95% CI 0.92–1.01) and non-mRNA vaccines (RR 0.84, 95% CI 0.76–0.93).

A sensitivity analysis was conducted according to the study- and patient-level categorical characteristics to account for heterogeneity in seroconversion observed after the first and second doses of COVID-19 vaccine. When studies of PLWH including inactivated virus vaccines or PLWH receiving antiretroviral therapy (ART) were excluded, a subgroup analysis was performed for studies involving noninactivated virus vaccines after both the first and the second dose. After the first dose, no significant difference was found in effects on seroconversion between PLWH and healthy controls (RR 0.98, 0.89–1.07,  $I^2 = 0\%$ , Figure S1). After the second dose, there was a significant difference in the effects on seroconversion between PLWH and healthy controls (RR 0.92, 0.86–0.98,  $I^2 = 92\%$ , Figure S2). Therefore, the COVID-19 vaccine platforms might be a confounder.

The brand of serology kit for assays and country/region of the study were of inconsistent significance across PLWH groups and are therefore unlikely to be major confounders overall.

The mixed-effects meta-regression of seroconversion against potential effect moderators (continuous and categorical study level characteristics), including mean age of patients, brand of serology kit, time points for assays after COVID-19 vaccination, and risk of bias of study, showed no consistent effect moderation across PLWH after both the first or the second dose.

All studies included in our meta-analysis involved healthy controls to improve comparability of data, and responses in healthy controls were homogenous across studies.

**Table 1**  
Characteristics of included studies.

Source	Vaccine	n, Population(s) of interest	Age <sup>a</sup>	Gender <sup>b</sup>	Country/Region	n, Comparison	Immunoassay	Threshold for positive response	Endpoints of data collection
Zou et al. (2022)	WIBP-CorV (inactivated)	46, HIV patients	Patients: 36 (31, 42) Controls: 31(27, 39)	Patients: 40/46 (87%) Controls: 19/38 (50%)	China	38, healthy controls	The serum levels of nAbs against the S protein RBD determined by SARS-CoV-2 nAbs assay kit by surrogate virus neutralization test (Zhuhai Livzon Diagnostics Inc, Zhuhai, China)	Positive serology: RBD: ≥10 BAU/ml	Day 28 after 2nd dose
Zeng et al. (2022)	BIBP-CorV or CoronaVac (inactivated)	132, HIV patients	Patients: 32 (28, 39) Controls: 34 (29, 39)	Patients: 119/132 (90.2%) Controls: 115/130 (75.5%)	China	130, healthy controls	S-RBD-IgG detected by magnetic particle chemiluminescence kits (Shengxiang Biotechnology, Changsha, China)	Positive serology: RBD: ≥1.0	Day 28 and 180 after 2nd dose
Madhi et al. (2022)	NVX-CoV2373 (recombinant protein nanoparticle)	122, HIV patients	Patients: 39 (34, 44) Controls: 32 (26, 38)	Patients: 37/122 (30.3%) Controls: 1217/2089 (58.3%)	South Africa	2089, healthy controls	Anti-S-IgG antibodies	Positive serology: > 95% participants in the placebo group	Day 14 after 2nd dose
Huang et al. (2022)	Sinopharm and Sinovac CoronaVac (inactivated)	129, HIV patients	Patients: 34 (28, 38) Controls: 34 (29, 47)	Patients: 128/129 (99.2%) Controls: 40/53 (75.5%)	China	53, healthy controls	SARS-CoV-2 specific total antibody and S-IgG antibodies using Chemiluminescence assay (CLIA) kits (Beijing Wantai Biological Pharmacy Enterprise Co., Ltd., Beijing, China)	Positive serology: > 30 pg/ml	Day 15–28 after 2nd dose
Antinori et al. (2022)	BNT162b2 or mRNA-1273 (mRNA)	166, HIV patients	Patients: 55 (46, 59) Controls: 42 (32, 53)	Patients: 27/166 (16.3%) Controls: 48/169 (28.4%)	Italy	169, healthy controls	The SARS-CoV-2 specific anti-N, and the anti-S/RBD tests (ARCHITECT SARS-CoV-2 IgG, and ARCHITECT SARS-CoV-2 IgG II) Quantitative, Abbott Laboratories, Wiesbaden, Germany respectively)	Positive serology: nAB ≥10	Day 28 after 2nd dose
Lombardi et al. (2022)	mRNA-1273 (mRNA)	71, HIV patients	Patients: 47 (39, 55) Controls: 58 (50, 66)	Patients: 60/71 (84.5%) Controls: 7/10 (70%)	Italy	10, healthy controls	Electrochemi Luminescent Immuno Assay (ECLIA)	Not explicitly stated	Day 28 from first dose and day 28 after 2nd dose
Schmidt et al. (2022)	BNT162,b2 (mRNA)	50, HIV patients	Patients: 55 (46–60) Controls: 42 (30–53)	Patients: 34/50 (68%) Controls: 32/60 (53.3%)	Germany	60, healthy controls	CE certified commercial ELISA (Euroimmun, Lübeck, Germany)	Positive serology: RBD: >1.1	7–155 days after the second dose (median of 37 days for people living with HIV and 26 days for controls)
Ogbe et al. (2022)	AZD1222 (Viral vector)	54, HIV patients	Patients: 42.5 (37.2–49.8) Controls: 38.5 (29.2–45.0)	Patients: 54/54 (100%) Controls: 36/50 (72%)	UK	60, healthy controls	Standardized total IgG ELISA against trimeric SARS-CoV-2 S protein	Seropositive: >3-fold increase	Day 42 and day 182 after 2nd dose
Brumme et al. (2022)	BNT162b2, mRNA-1273, AZD1222 (Viral vector)	100, HIV patients	Patients: 54 (40–61) Controls: 47 (35–70)	Patients: 88/100 (88%) Controls: 50/152 (33%)	Canada	152, healthy controls	Electro-chemiluminescence sandwich immunoassays	Not explicitly stated	One month after the first dose, and at 1 and 3 months after 2nd dose
Heftdal et al. (2022)	BNT162,b2 (mRNA)	269, HIV patients	Patients: 56.0 (49–64) Controls: 56 (49–63)	Patients: 242/269 (90.0%) Controls: 73/538 (13.6%)	Denmark	538, healthy controls	An in-house ELISA that detects IgG antibodies against the RBD of SARS-CoV-2	Positive serology: >150 AU/ml	Three weeks and 2 months after the first dose

**Table 1** (continued)

Source	Vaccine	n, Population(s) of interest	Age <sup>a</sup>	Gender <sup>b</sup>	Country/Region	n, Comparison	Immunoassay	Threshold for positive response	Endpoints of data collection
<a href="#">Feng et al. (2022)</a>	BIBP-CorV (inactivated)	42, HIV patients	Patients: 42.74 (10.17) Controls: 37.79 (8.8)	Patients: 29/42 (69%) Controls: 16/28 (57.1%)	China	28, healthy controls	An in-house ELISA that detects IgG antibodies against the RBD of SARS-CoV-2	Seropositive: >3-fold increase	Four weeks after the first dose and 4 weeks after 2nd dose
<a href="#">Khan et al. (2021)</a>	Ad26.CoV2.S (Viral vector)	8, HIV patients	Patients: 47 (42-51) Controls: 46 (40-52)	Patients: 0 (0%) Controls: 2/49 (4.1%)	South African	24, healthy controls	ImmuSAFE COVID-19 Array slides (Sengenics Corporation, Singapore) to measure the anti-SARS-CoV-2 IgG antibodies against SARS-CoV-2 N	The mean plus 2 SD of pre-pandemic control signal	Six-ten weeks after the first dose
<a href="#">Lv et al. (2022)</a>	CoronaVac (inactivated) BBIBP-CorV (inactivated)	24, HIV patients	Patients: 44 (34-54) Controls: 37 (16-58)	Patients: 12/24 (50%) Controls: 15/24 (62.5%)	China	24, healthy controls	A competitive ELISA kit to measure anti-SARS-CoV-2 neutralization antibodies	Not explicitly stated	About 40 days after 2nd dose
<a href="#">Tuan et al. (2022)</a>	BNT162,b2 (mRNA)	45, HIV patients	Patients: 61 (55-80) Controls: 61 (55-80)	Patients: 30/45 (67%) Controls: 21/33 (64%)	USA	23, healthy controls	Healgen (Houston, TX, USA) COVID-19 anti-S-IgG/IgM Rapid Test Cassette	Not explicitly stated	Three weeks after the first dose (and prior to receipt of the second dose) and at 2-3 weeks after 2nd dose
<a href="#">Bergman et al. (2021)</a>	BNT162,b2 (mRNA)	90, HIV patients	Patients: >18 Controls: >18	Patients: 54/90 (60%) Controls: 39/90 (43%)	Sweden	90, healthy controls	Quantitative Roche Elecsys anti-SARS-CoV-2 S enzyme immunoassay	Positive serology: >0.79 U/ml	Forteen days after 2nd dose
<a href="#">Netto et al. (2022)</a>	CoronaVac (inactivated)	215, HIV patients	Patients: 54 (45-60) Controls: 48 (37-58)	Patients: 135/215 (60%) Controls: 109/296 (37%)	Brazil	296, healthy controls	IgG antibodies targeting S1 and 2 proteins in the receptor binding domain (Indirect ELISA, LIAISON SARS-CoV-2 S1/S2 IgG, DiaSorin, Italy), and the virusNab detection assay SARS-CoV-2 sVNT RBD-HRP Kit (GenScript, Piscataway, NJ, USA)	Positive serology: ≥15.0 AU/μl	Six weeks (day 69) after 2nd dose
<a href="#">Frater et al. (2021)</a>	AZD1222 (Viral vector)	54, HIV patients	Patients: 42.5 (37.2-49.8) Controls: 38.5 (29.2-45.0)	Patients: 54/54 (100%) Controls: 26/50 (52%)	UK	50, healthy controls	Standardized total IgG ELISA against trimeric SARS-CoV-2 S protein	Not explicitly stated	Days 42 and 56 after 2nd dose
<a href="#">Rahav et al. (2021)</a>	BNT162,b2 (mRNA)	156, HIV patients	Patients: 49 (42-57)	137 (87.8%)	Israel	272, healthy controls	VSV-S SARS-CoV-2 pseudo-virus neutralization assay (Gert Zimmer)	Positive serology: RBD: >1.1	Thirty days after 2nd dose
<a href="#">Jedicke et al. (2022)</a>	BNT162,b2 (mRNA)	88, HIV patients	Patients: Mean (range): 53.5 (26-86) Controls: Mean (range): 44 (23-61)	Patients: 86/88 (97.7%) Controls: 32/41 (78.0%)	Germany	41, healthy controls	ELISA (QuantiVac; Euroimmun, Lübeck, Germany)	Not explicitly stated	Mean of 18.7 days (range 0-42 days) after the first and 35 days (range 1-128 days) after the boost vaccination.
<a href="#">Levy et al. (2021)</a>	BNT162,b2 (mRNA)	143, HIV patients	Patients: Mean (sd): 49.8 (11.6) Controls: Mean (sd): 55.8 (14.3)	Patients: 131/143 (91.6%) Controls: 66/261 (25.3%)	Israel	261, healthy controls	ELISA that detects IgG antibodies against the RBD of SARS-CoV-2	Positive serology: >1.1	Two-three weeks following 2nd dose

(continued on next page)

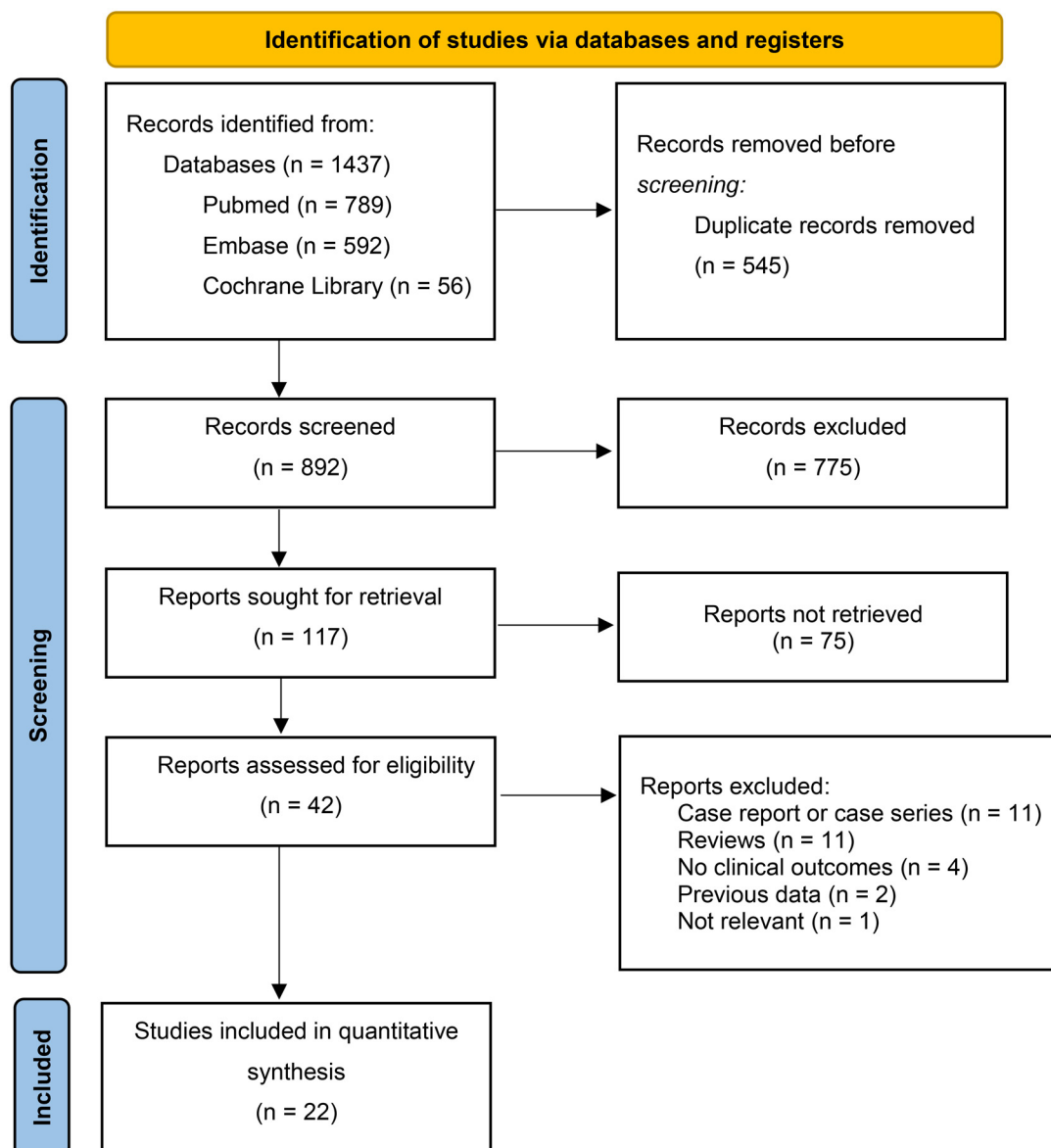
**Table 1** (continued)

Source	Vaccine	n, Population(s) of interest	Age <sup>a</sup>	Gender <sup>b</sup>	Country/Region	n, Comparison	Immunoassay	Threshold for positive response	Endpoints of data collection
Madhi et al. (2021)	AZD1222 (Viral vector)	52, HIV patients	Patients: 37 (32–45) Controls: 34 (23–41)	Patients: 16/52 (31%) Controls: 17/29 (59%)	South Africa	29, healthy controls	Singleplex bead-based immunoassays were developed on the Luminex platform to quantitatively measure serum IgG binding to fibroblast-like synoviocytes and RBD	Seropositive: >2-fold increase	Day 28 from first dose and 14 days post booster
Woldemeskel et al. (2021)	BNT162,b2 (mRNA)	12, HIV patients	Patients: Median (range): 52 (25–59) Controls: Median (range): 41 (24–59)	Patients: 5/12 (41.7%) Controls: 10/17 (58.8%)	USA	17, healthy controls	Euroimmun Anti-SARS-CoV-2 IgG ELISA	Not stated	Between 7 and 17 days after 2nd dose

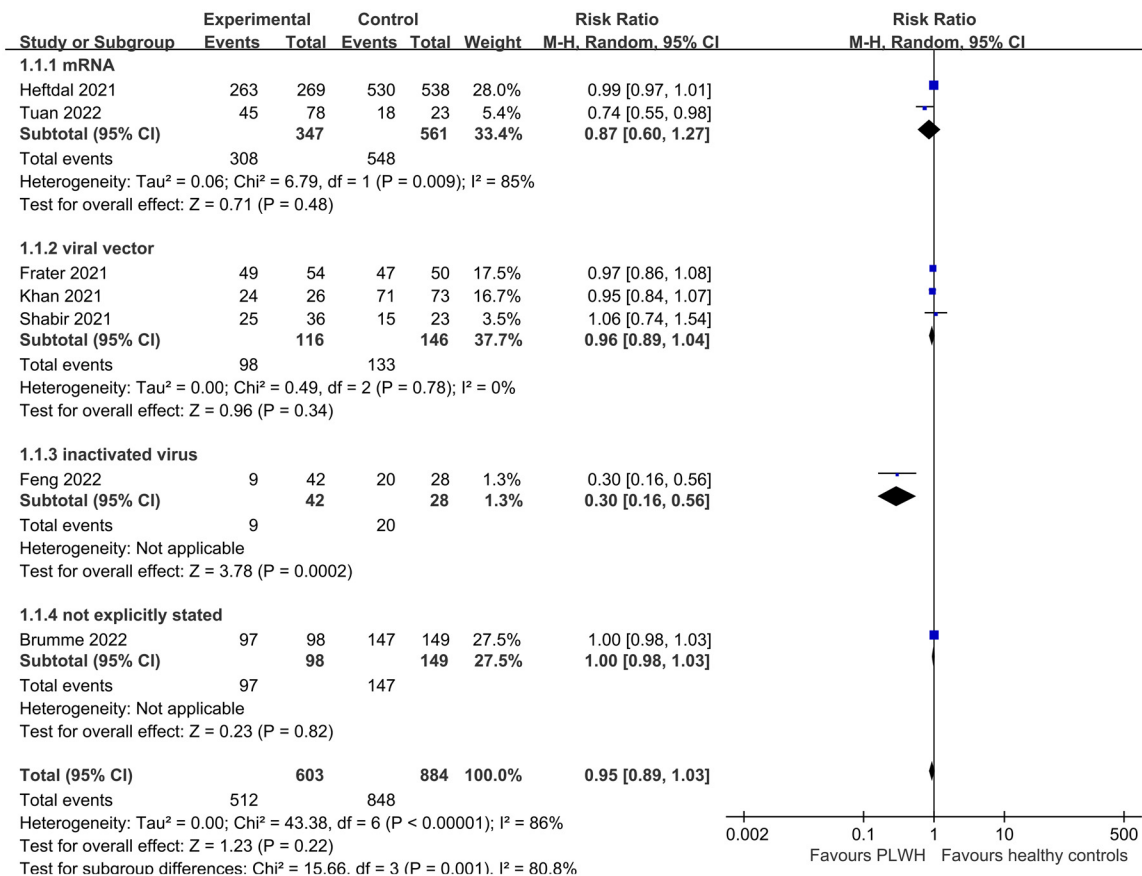
Abbreviations: BAU, binding antibody units; ELISA, enzyme-linked immunosorbent assay; Ig, immunoglobulin; IQR, interquartile range; nAb, neutralizing antibodies; N, nucleocapsid; RBD, receptor binding domain; S, spike.

<sup>a</sup> Reported as median (IQR) unless otherwise stated.

<sup>b</sup> Reported as percentage of males unless otherwise stated.



**Figure 1.** Flowchart of study selection.



**Figure 2.** Pooled risk ratios for PLWH compared with healthy controls after a first dose of COVID-19. Abbreviations: M-H, Mantel-Haenszel; mRNA, messenger RNA; PLWH; people living with HIV.

**Quality assessment**

A total of 20 (91%) studies were assessed to be at low risk of bias and two (9%) at moderate risk of bias (Table S3). No studies were considered to be at severe or critical risk of bias. The risk of bias was mainly associated with confounding effects, with controls not being age-matched or with recruited patients lacking available data at predetermined end points. The publication bias evaluation results showed that the funnel plot was generally symmetrical by visual inspection. Therefore, no significant publication bias was found in our study (Figure S3).

**Discussion**

This review is the first to assess and compare the efficacy of COVID-19 vaccines available at present in PLWH compared to the general population. In this systematic review and meta-analysis of 22 studies, we found that PLWH had a slightly lower seroconversion after a first and second dose of COVID-19 vaccine than healthy controls. The pooled RR for seroconversion after the first vaccine dose was lower among PLWH than healthy controls; however, there was no statistical significance between the two groups (RR 0.95, 95% CI 0.89-1.03, I<sup>2</sup> = 86%). Antibody response among PLWH improved significantly after the second dose (86.4%), but the response of the control group was more pronounced (92.2%). Therefore, the pooled RR after the second dose decreased to 0.92 among PLWH. Although the seroconversion was slightly lower after the first dose among PLWH than healthy controls, the immune response to COVID-19 vaccines was shown to be preserved after the second dose, which is consistent with one previous research (Lee et al., 2022). Hyperviremia may lead to a shortened half-life of the

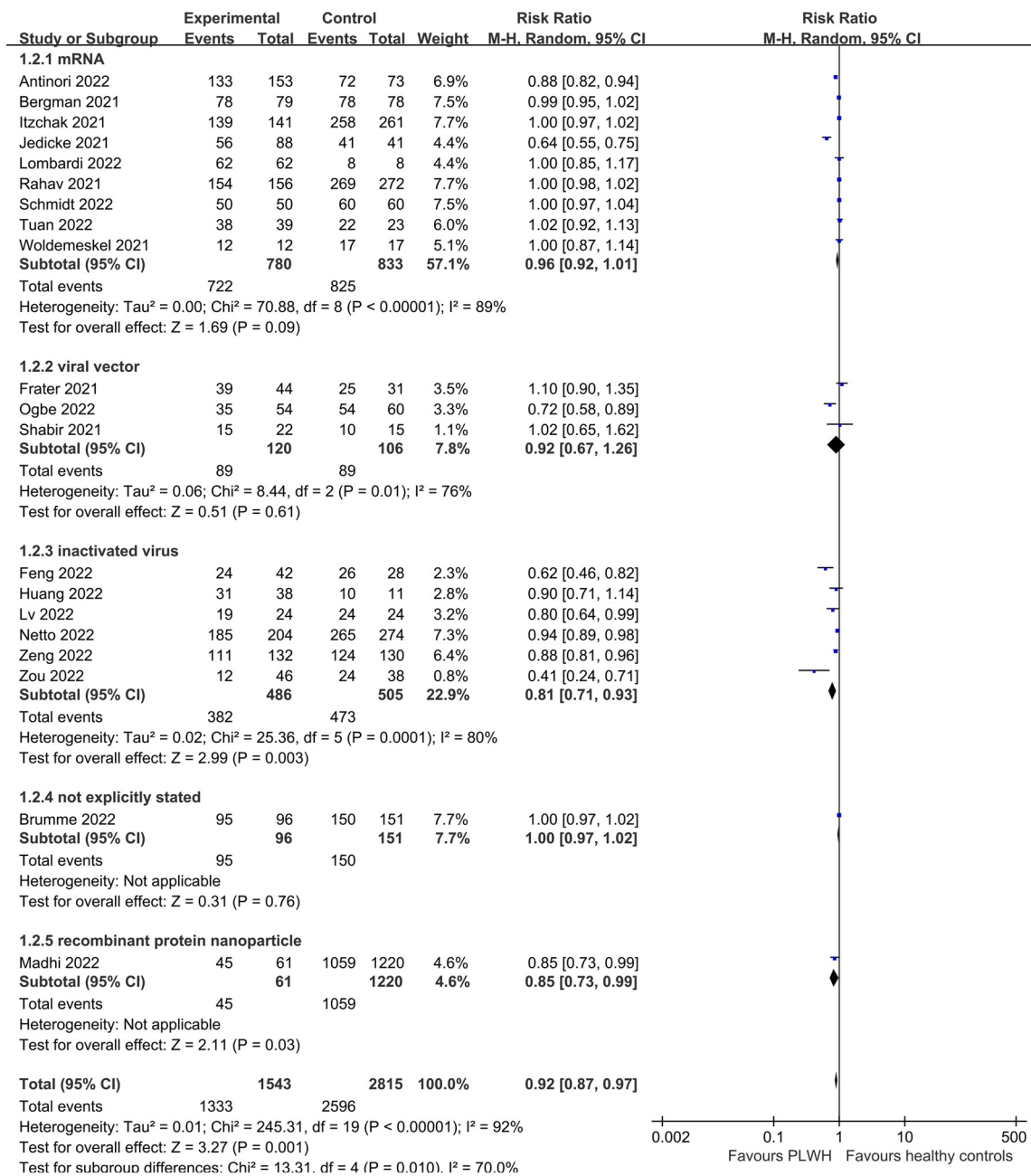
COVID-19 vaccines, which is why the subpopulations of PLWH may require repeated vaccination (Oyelade et al., 2022).

The benefits of additional doses and boosters of vaccines are well established, both for COVID-19 (Doria-Rose et al., 2021; Livingston, 2021; Voysey et al., 2021) and for pre-existing vaccines, such as pneumococcal vaccine (Duarte et al., 2022) and inactivated Hantaan virus vaccine (Hantavax®) (Song et al., 2020). Our findings similarly highlight the importance of a second dose of the COVID-19 vaccine for PLWH. Across the included studies, a second dose of the COVID-19 vaccine was associated with greatly improved seroconversion and antibody titer levels, with increasing immunogenicity and protection in PLWH.

Among PLWH, our results show no ideal but favorable seroconversion rate, even after a second dose of COVID-19 vaccine, prompting the requirement for additional measures (e.g., booster vaccination). Lapointe et al. showed that in PLWH, the humoral response after the third dose greatly exceeded the level after the second dose, especially for the mRNA-1273 vaccine (Moderna, Cambridge, MA, USA) (Lapointe et al., 2022). In an observational study, Barda et al. (2021) showed that a third dose of the BNT162b2 vaccine was effective in protecting individuals against severe COVID-19-related outcomes, compared with receiving only two doses at least 5 months before. In August 2021, the US Food and Drug Administration approved a third dose of Pfizer-BioNTech and Moderna vaccines for PLWH populations, with other countries following suit (Wise, 2021).

Our meta-analyses show significant heterogeneity in immunogenicity between different PLWH groups after both the first and the second dose of COVID-19 vaccines. After the vaccination, the response noticeably varied in PLWH, which may be attributed to the diversity of anti-HIV drugs, or the widespread COVID-19 vac-





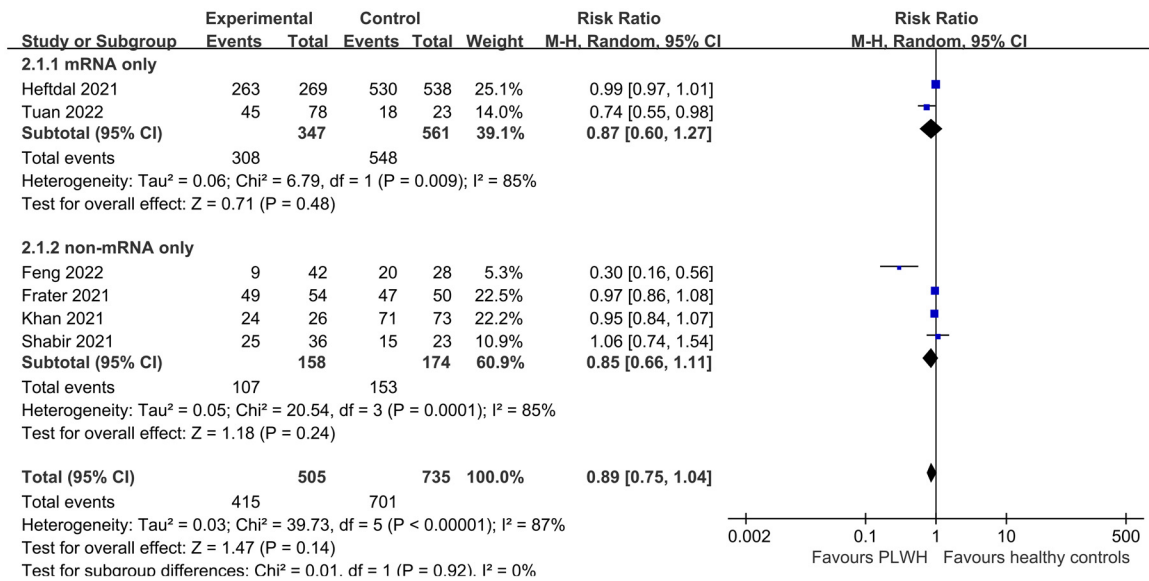
**Figure 3.** Pooled risk ratios for PLWH compared with healthy controls after a second dose of COVID-19. Abbreviations: M-H, Mantel-Haenszel; mRNA, messenger RNA; PLWH; people living with HIV.

cinations resulted from the release of a multisociety joint statement advocating vaccination for all PLWH midway through several of the reported studies (Mohammed et al., 2020). Vaccine regimes should be tailored according to the kinds of anti-HIV drugs and the disease severity. One of the included studies found that robust humoral immunity was triggered in the majority of PLWH receiving ART after a full BNT162b2 vaccination; however, controls who were HIV-negative produced significantly higher mean anti-spike IgG concentrations with less variability (Jedicke et al., 2022).

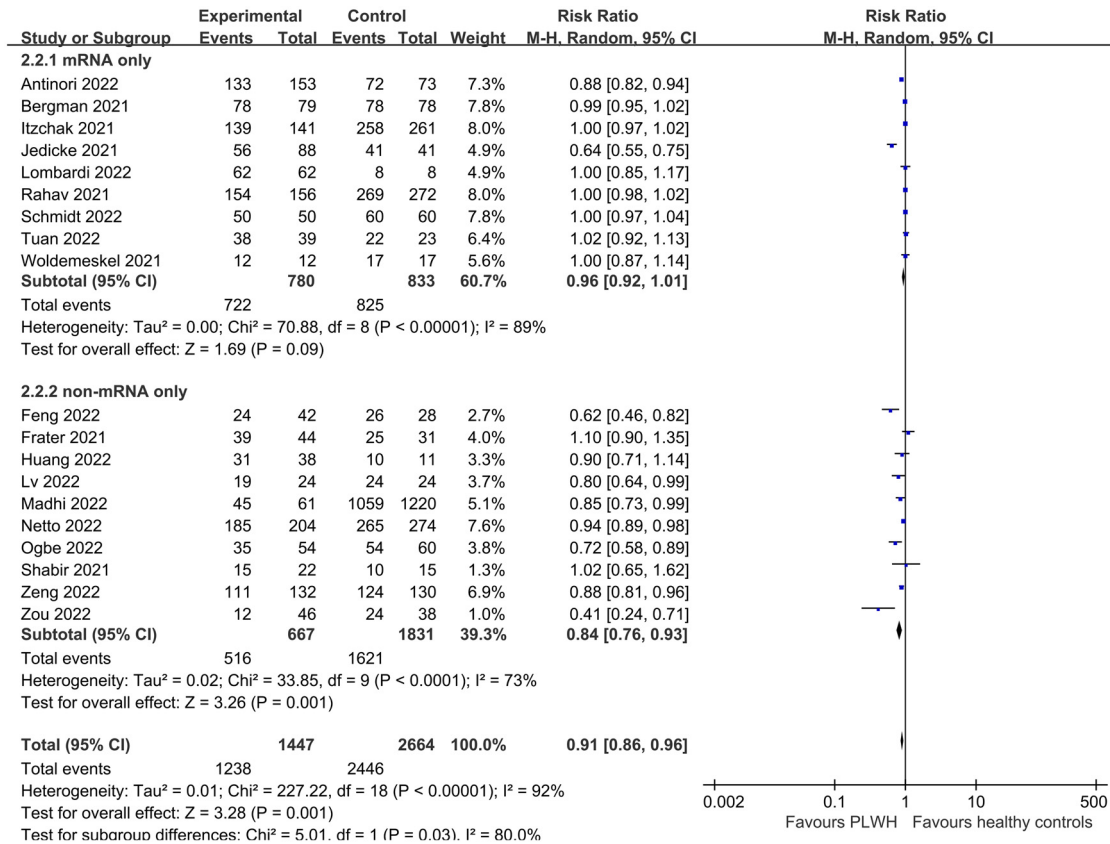
Currently, there is no international consensus on the measures to determine immunogenicity. Surrogate measures, including seroconversion rates and geometric mean titers, were reported by many trials. These surrogate measures involved parameters related to recombinant 2019-nCoV spike, receptor binding domain, or neutralizing IgG or total antibodies. The use of immunomarkers to

predict protection against COVID-19 has been the subject of debate (Earle et al., 2021; Garcia-Beltran et al., 2021; Jin et al., 2021; Khoury et al., 2021; Roozendaal et al., 2021; Vidal et al., 2021). The neutralizing antibody level has more recently been recognized as a reliable predictor of protection against symptomatic COVID-19; however, the measures used in many studies varied. In this systematic review, only studies that compared measures of effect between PLWH and healthy controls were included.

There are various studies that compare the immunogenicity of other vaccines between PLW HIV/AIDS and healthy individuals. Studies have established that hepatitis B, influenza, and pneumococcal conjugate vaccines have lower response rates in PLWH, which makes it necessary to study COVID-19 vaccines in PLWH (Boey et al., 2021; Lee et al., 2020; Nunes et al., 2020; Pallikkuth et al., 2018; Whitaker et al., 2012). In view of the HIV/AIDS spec-



**Figure 4.** Subgroup analysis of vaccine type among PLWH patients after first dose. Abbreviations: M-H, Mantel-Haenszel; mRNA, messenger RNA; PLWH; people living with HIV.



**Figure 5.** Subgroup analysis of vaccine type among PLWH patients after second dose. Abbreviations: M-H, Mantel-Haenszel; mRNA, messenger RNA; PLWH; people living with HIV.

trum, the effect of CD4 count reduction on immune response remains to be determined. Data on patients with PLWH are rare (Amodio et al., 2021). However, even patients with primary antibody deficiencies, such as combined variable immunodeficiency, have developed antispikes antibodies after COVID-19 vaccination (Delmonte et al., 2021; Hagin et al., 2021). Therefore, immunization against COVID-19 may be particularly important for all PLWH.

Over the last decade, mRNA has emerged as a promising platform for developing vaccines against infectious diseases and cancer (Pardi et al., 2018). Compared with traditional vaccines, such as live attenuated vaccines, inactivated virus vaccines, and protein subunit vaccines, mRNA vaccines have the advantages of versatility, rapid development, good safety profiles, and potent immunogenicity (Alberer et al., 2017; Corbett et al., 2020; de Jong et al., 2019; Feldman et al., 2019; Gay et al., 2018). Therefore, multiple

researchers and companies have chosen this platform to develop vaccines against COVID-19. It is difficult to directly compare seroconversion rates of the COVID-19 mRNA vaccines with more traditional, frequently used vaccines. In our study, no significant difference was found in a subgroup analysis of mRNA *versus* conventional vaccines in PLWH. A systematic review by Fan *et al.* (2021), which compared mRNA vaccines with conventional vaccines in patients without HIV, summarized the safety and efficacy of the three main COVID-19 vaccine platforms (mRNA, nonreplicating viral vector, inactivated) reported in phase III trials. In terms of vaccine safety, mRNA vaccines showed more relevance to serious adverse events than the other two vaccine platforms, but no solid evidence indicated that COVID-19 vaccines directly caused serious adverse events. A network meta-analysis suggests that the immune response to the influenza vaccine might not be as robust in PLWH, but they appear to benefit from vaccination (Zhang *et al.*, 2018). These findings reflect the current situation with COVID-19 and vaccination.

This study has several limitations. First, most of the enrolled studies are observational, but two are randomized controlled trials. Factors that might influence the immune response to the vaccine, such as differences in study design and sample size, might not be controlled for between PLWH group and the healthy control group. In addition, our findings did not control for CD4+ T-cell count and ART treatment. To deal with this limitation, we performed subgroup analysis and found that there was no significant effect modification between studies with different designs. Second, in our study, the rate of seroconversion was pooled after the first and second doses of a COVID-19 vaccine. However, the seroconversion rate is an indicator of an immune response to a vaccine; it is only a proxy for the effects of the vaccine on infection rates and COVID-19 severity. Data on clinical efficacy end points, such as COVID-19 infection rates in vaccinated PLWH, are still lacking. Third, we did not check the different studies including the same patients (e.g., once as an intervention group and then as a control). Last, the results may be imbalanced because nine of the 17 publications enrolled were on BNT162b2. In addition, vaccine type might affect seroconversion rates after COVID-19 vaccination. However, because the studies included in this review predominantly used mRNA vaccines, the possible differential analyses were limited.

## Conclusion

In conclusion, this meta-analysis shows that, COVID-19 vaccines show favorable immunogenicity and efficacy in PLWH compared with healthy individuals. A second dose was associated with consistently improved seroconversion; although, it is slightly lower in PLWH than in healthy individuals. Additional strategies, such as the administration of a third (booster) vaccination with mRNA COVID-19 vaccines, might improve seroprotection for these patients. Moreover, our results suggest that policymakers, health planners, and other stakeholders should encourage COVID-19 vaccine uptake by providing trusted information and addressing COVID-19 vaccine hesitancy in PLWH.

## Declaration of competing interest

The authors have no competing interests to declare.

## Funding

This work was supported by the Science and Technology Department of Henan Province (No. 112102310306) and Science and Technology Bureau of Kaifeng (No. 119).

## Ethical approval statement

Not applicable.

## Acknowledgments

The authors would like to acknowledge Naiqin Wang for assessing the quality of the included studies.

## Author contributions

JY and YC contributed equally to this paper and are joint first authors. CW and XZ contributed equally to this paper and are joint last authors. JY, CW, and YC conceived and designed the study. JY and YC selected the articles and extracted data. JY and CW were responsible for statistical analysis. JY and YL wrote the first draft of the manuscript. CW, XZ, and YL provided advice at different stages. All authors approved the final version of the manuscript. JY is the guarantor. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

## Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

## Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:[10.1016/j.ijid.2022.10.005](https://doi.org/10.1016/j.ijid.2022.10.005).

## References

- Alberer M, Gnad-Vogt U, Hong HS, Mehr KT, Backert L, Finak G, et al. Safety and immunogenicity of a mRNA rabies vaccine in healthy adults: an open-label, non-randomised, prospective, first-in-human phase 1 clinical trial. *Lancet* 2017;390:1511–20.
- Amodio D, Ruggiero A, Sgrulletti M, Pighi C, Cotugno N, Medri C, et al. Humoral and cellular response following vaccination with the BNT162b2 mRNA COVID-19 vaccine in patients affected by primary immunodeficiencies. *Front Immunol* 2021;12.
- Antinori A, Cicalini S, Meschi S, Bordoni V, Lorenzini P, Vergori A, et al. Humoral and cellular immune response elicited by mRNA vaccination against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in people living with human immunodeficiency virus receiving antiretroviral therapy based on current CD4 T-lymphocyte count. *Clin Infect Dis* 2022;75:e552–63.
- 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.
- Barda N, Dagan N, Cohen C, Hernán MA, Lipsitch M, Kohane IS, et al. Effectiveness of a third dose of the BNT162b2 mRNA COVID-19 vaccine for preventing severe outcomes in Israel: an observational study. *Lancet* 2021;398:2093–100.
- Bergman P, Blennow O, Hansson L, Mielke S, Nowak P, Chen P, et al. Safety and efficacy of the mRNA BNT162b2 vaccine against SARS-CoV-2 in five groups of immunocompromised patients and healthy controls in a prospective open-label clinical trial. *Ebiomedicine* 2021;74.
- Berlin DA, Gulick RM, Martinez FJ. Severe Covid-19. *N Engl J Med* 2020;383:2451–60.
- Boey L, Curinckx A, Roelants M, Derdelinckx I, Van Wijngaerden E, De Munter P, et al. Immunogenicity and safety of the 9-valent human papillomavirus vaccine in solid organ transplant recipients and adults infected with human immunodeficiency virus (HIV). *Clin Infect Dis* 2021;73:e661–71.
- Brumme ZL, Mwimanzu F, Lapointe HR, Cheung PK, Sang Y, Duncan MC, et al. Humoral immune responses to COVID-19 vaccination in people living with HIV receiving suppressive antiretroviral therapy. *npj Vaccines* 2022;7:28.
- Cederwall S, Pählman LI. Respiratory adenovirus infections in immunocompetent and immunocompromised adult patients. *Epidemiol Infect* 2020;147:e328.
- Corbett KS, Flynn B, Foulds KE, Francica JR, Boyoglu-Barnum S, Werner AP, et al. Evaluation of the mRNA-1273 vaccine against SARS-CoV-2 in nonhuman Primates. *N Engl J Med* 2020;383:1544–55.
- Couch RB, Englund JA, Whimby E. Respiratory viral infections in immunocompetent and immunocompromised persons. *Am J Med* 1997;102:2–9.
- de Jong W, Aerts J, Allard S, Brander C, Buyze J, Florence E, et al. iHIVARNA phase IIa, a randomized, placebo-controlled, double-blinded trial to evaluate the safety and immunogenicity of iHIVARNA-01 in chronically HIV-infected patients under stable combined antiretroviral therapy. *Trials* 2019;20:361.

- Delmonte OM, Bergerson JRE, Burbelo PD, Durkee-Shock JR, Dobbs K, Bosticardo M, et al. Antibody responses to the SARS-CoV-2 vaccine in individuals with various inborn errors of immunity. *J Allergy Clin Immunol* 2021;148:1192–7.
- Doria-Rose N, Suthar MS, Makowski M, O'Connell S, McDermott AB, Flach B, et al. Antibody persistence through 6 months after the second dose of mRNA-1273 vaccine for Covid-19. *N Engl J Med* 2021;384:2259–61.
- Duarte G, Muresan P, Ward S, Laimon L, Pelton SI, Canniff J, et al. Immunogenicity of conjugated and polysaccharide pneumococcal vaccines administered during pregnancy or postpartum to women with HIV. *J Infect Dis* 2022;225:1021–31.
- Earle KA, Ambrosino DM, Fiore-Gartland A, Goldblatt D, Gilbert PB, Siber GR, et al. Evidence for antibody as a protective correlate for COVID-19 vaccines. *Vaccine* 2021;39:4423–8.
- Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. *BMJ* 1997;315:629–34.
- Eyre DW, Lumley SF, Wei J, Cox S, James T, Justice A, et al. Quantitative SARS-CoV-2 anti-spike responses to Pfizer-BioNTech and Oxford-AstraZeneca vaccines by previous infection status. *Clin Microbiol Infect* 2021;27 1516.e7–1516.e14.
- Fan YJ, Chan KH, Hung IF. Safety and efficacy of COVID-19 vaccines: a systematic review and meta-analysis of different vaccines at Phase 3. *Vaccines (Basel)* 2021;9:989.
- Feldman RA, Fuhr R, Smolenov I, Mick Ribeiro A, Panther L, Watson M, et al. mRNA vaccines against H10N8 and H7N9 influenza viruses of pandemic potential are immunogenic and well tolerated in healthy adults in phase 1 randomized clinical trials. *Vaccine* 2019;37:3326–34.
- Feng Y, Zhang Y, He Z, Huang H, Tian X, Wang G, et al. Immunogenicity of an inactivated SARS-CoV-2 vaccine in people living with HIV-1: a non-randomized cohort study. *Eclinicalmedicine* 2022;43.
- 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.
- Garcia-Beltran WF, Lam EC, Astudillo MG, Yang D, Miller TE, Feldman J, et al. COVID-19-neutralizing antibodies predict disease severity and survival. *Cell* 2021;184:476–88 e11.
- Gay CL, DeBenedette MA, Tcherepanova IY, Gamble A, Lewis WE, Cope AB, et al. Immunogenicity of AGS-004 dendritic cell therapy in patients treated during acute HIV infection. *AIDS Res Hum Retroviruses* 2018;34:111–22.
- González de Aledo M, Cañizares A, Vázquez-Rodríguez P, Castro Á, Moldes L, López S, et al. Safety and immunogenicity of SARS-CoV-2 vaccines in people with HIV. *AIDS* 2022;36:691–5.
- Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ* 2008;336:924–6.
- Hagin D, Freund T, Navon M, Halperin T, Adir D, Marom R, et al. Immunogenicity of Pfizer-BioNTech COVID-19 vaccine in patients with inborn errors of immunity. *J Allergy Clin Immunol* 2021;148:739–49.
- Heftdal LD, Knudsen AD, Hamm SR, Hansen CB, Møller DL, Pries-Heje M, et al. Humoral response to two doses of BNT162b2 vaccination in people with HIV. *J Intern Med* 2022;291:513–18.
- Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. *Stat Med* 2002;21:1539–58.
- Huang X, Yan Y, Su B, Xiao D, Yu M, Jin X, et al. Comparing immune responses to inactivated vaccines against SARS-CoV-2 between people living with HIV and HIV-negative individuals: a cross-sectional study in China. *Viruses* 2022;14:277.
- 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.
- Jin P, Li J, Pan H, Wu Y, Zhu F. Immunological surrogate endpoints of COVID-2019 vaccines: the evidence we have versus the evidence we need. *Signal Transduct Target Ther* 2021;6:48.
- Khan K, Lustig G, Bernstein M, Archary D, Cele S, Karim F, et al. Immunogenicity of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and Ad26.COV2.S vaccination in people living with human immunodeficiency virus (HIV). *Clin Infect Dis* 2021;75:e857–64.
- Khoury DS, Cromer D, Reynaldi A, Schlub TE, Wheatley AK, Juno JA, et al. Neutralizing antibody levels are highly predictive of immune protection from symptomatic SARS-CoV-2 infection. *Nat Med* 2021;27:1205–11.
- Kyriakidis NC, López-Cortés A, González EV, Grimaldos AB, Prado EO. SARS-CoV-2 vaccines strategies: a comprehensive review of phase 3 candidates. *npj Vaccines* 2021;6:28.
- Lapointe HR, Mwimanzu F, Cheung PK, Sang Y, Yaseen F, Umvilighozo 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* 2022;jiac229.
- Lee JH, Hong S, Im JH, Lee JS, Baek JH, Kwon HY. Systematic review and meta-analysis of immune response of double dose of hepatitis B vaccination in HIV-infected patients. *Vaccine* 2020;38:3995–4000.
- Lee ARYB, Wong SY, Chai LYA, Lee SC, Lee MX, Muthiah MD, et al. Efficacy of covid-19 vaccines in immunocompromised patients: systematic review and meta-analysis. *BMJ* 2022;376.
- Levy I, Wieder-Finesod A, Litchevsky V, Biber A, Indenbaum V, Olmer L, et al. Immunogenicity and safety of the BNT162b2 mRNA COVID-19 vaccine in people living with HIV-1. *Clin Microbiol Infect* 2021;27:1851–5.
- Livingston EH. Necessity of 2 doses of the Pfizer and moderna COVID-19 vaccines. *JAMA* 2021;325:898.
- Lombardi A, Butta GM, Donnici L, Bozzi G, Oggioni M, Bono P, et al. Anti-spike antibodies and neutralising antibody activity in people living with HIV vaccinated with COVID-19 mRNA-1273 vaccine: a prospective single-centre cohort study. *Lancet Reg Health Eur* 2022;13.
- Lv Z, Li Q, Feng Z, Zheng X, NaYin YH, et al. Inactivated SARS-CoV-2 vaccines elicit immunogenicity and T-cell responses in people living with HIV. *Int Immunopharmacol* 2022;102.
- Madhi SA, Koen AL, Izu A, Fairlie L, Cutland CL, Baillie V, et al. Safety and immunogenicity of the ChAdOx1 nCoV-19 (AZD1222) vaccine against SARS-CoV-2 in people living with and without HIV in South Africa: an interim analysis of a randomised, double-blind, placebo-controlled, phase 1B/2A trial. *Lancet HIV* 2021;8:e568–80.
- Madhi SA, Moodley D, Hanley S, Archary M, Hoosain Z, Laloo 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.
- Mallapaty S. China's COVID vaccines have been crucial - now immunity is waning. *Nature* 2021;598:398–9.
- Manuel O, Estabrook M. RNA respiratory viral infections in solid organ transplant recipients: guidelines from the American Society of Transplantation Infectious Diseases Community of Practice. *Clin Transplant* 2019;33:e13511.
- Merad M, Blish CA, Sallusto F, Iwasaki A. The immunology and immunopathology of COVID-19. *Science* 2022;375:1122–7.
- Mohammed AH, Blebil A, Dujaili J, Rasool-Hassan BA. The risk and impact of COVID-19 pandemic on immunosuppressed patients: cancer, HIV, and solid organ transplant recipients. *AIDS Rev* 2020;22:151–7.
- Netto LC, Ibrahim KY, Picone CM, Alves APPS, Aniceto EV, Santiago MR, et al. Safety and immunogenicity of CoronaVac in people living with HIV: a prospective cohort study. *Lancet HIV* 2022;9:e323–31.
- Nunes MC, Cutland CL, Moultrie A, Jones S, Ortiz JR, Neuzil KM, et al. Immunogenicity and safety of different dosing schedules of trivalent inactivated influenza vaccine in pregnant women with HIV: a randomised controlled trial. *Lancet HIV* 2020;7:e91–e103.
- Ogbe A, Pace M, Bittaye M, Tipoe T, Adele S, Alagaratnam J, et al. Durability of ChAdOx1 nCoV-19 vaccination in people living with HIV. *JCI Insight* 2022;7.
- Oyelade T, Raya RP, Latief K. HIV infection and the implication for COVID-19 vaccination. *Public Health Chall* 2022;1:e14.
- Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 2021;372:n71.
- Pallikkuth S, De Armas LR, Pahwa R, Rinaldi S, George VK, Sanchez CM, et al. Impact of aging and HIV infection on serologic response to seasonal influenza vaccination. *AIDS* 2018;32:1085–94.
- Pardi N, Hogan MJ, Porter FW, Weissman D. mRNA vaccines - a new era in vaccinology. *Nat Rev Drug Discov* 2018;17:261–79.
- Picaluga PP, Di Guardo A, Lagni A, Lotti V, Diani E, Navari M, et al. COVID-19 vaccine: between myth and truth. *Vaccines (Basel)* 2022;10:349.
- Rahav G, Lustig Y, Lavee J, Benjamini O, Magen H, Hod T, et al. BNT162b2 mRNA COVID-19 vaccination in immunocompromised patients: a prospective cohort study. *Eclinicalmedicine* 2021;41.
- Remschmidt C, Wichmann O, Harder T. Influenza vaccination in HIV-infected individuals: systematic review and assessment of quality of evidence related to vaccine efficacy, effectiveness and safety. *Vaccine* 2014;32:5585–92.
- Roosendaal R, Solforosi L, Stieh DJ, Serroyen J, Straetemans R, Dari A, et al. SARS-CoV-2 binding and neutralizing antibody levels after Ad26.COV2.S vaccination predict durable protection in rhesus macaques. *Nat Commun* 2021;12:5877.
- Schmidt KG, Harrer EG, Tascilar K, Kübel S, El Kenz B, Hartmann F, et al. Characterization of serum and mucosal SARS-CoV-2-antibodies in HIV-1-infected subjects after BNT162b2 mRNA vaccination or SARS-CoV-2 infection. *Viruses* 2022;14:651.
- Silveira MM, Moreira GMSG, Mendonça M. DNA vaccines against COVID-19: perspectives and challenges. *Life Sci* 2021;267.
- Song JY, Jeong HW, Yun JW, Lee J, Woo HJ, Bae JY, et al. Immunogenicity and safety of a modified three-dose priming and booster schedule for the Hantaan virus vaccine (Hantavax): a multi-center phase III clinical trial in healthy adults. *Vaccine* 2020;38:8016–23.
- Ssentongo P, Heilbrunn ES, Ssentongo AE, Advani S, Chinchilli VM, Nunez JJ, et al. Epidemiology and outcomes of COVID-19 in HIV-infected individuals: a systematic review and meta-analysis. *Sci Rep* 2021;11:6283.
- Sterne JAC, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ* 2019;366:14898.
- Tian Y, Hua W, Wu Y, Zhang T, Wang W, Wu H, et al. Immune response to hepatitis B virus vaccine among people living with HIV: a meta-analysis. *Front Immunol* 2021;12.
- Tuan JJ, Zapata H, Critch-Gillfillan T, Ryall L, Turcotte B, Mutic S, et al. Qualitative assessment of anti-SARS-CoV-2 spike protein immunogenicity (quasi) after COVID-19 vaccination in older people living with HIV. *HIV Med* 2022;23:178–85.
- Vergnes JN. Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine. *N Engl J Med* 2021;384:1577.
- Vidal SJ, Collier AY, Yu J, McMahan K, Tostanoski LH, Ventura JD, et al. Correlates of neutralization against SARS-CoV-2 variants of concern by early pandemic sera. *J Virol* 2021;95.
- Voysey M, Costa Clemens SA, Madhi SA, Weckx LY, Folegatti PM, Aley PK, et al. Single-dose administration and the influence of the timing of the booster dose on immunogenicity and efficacy of ChAdOx1 nCoV-19 (AZD1222) vaccine: a pooled analysis of four randomised trials. *Lancet* 2021;397:881–91.

- Whitaker JA, Roupael NG, Edupuganti S, Lai L, Mulligan MJ. Strategies to increase responsiveness to hepatitis B vaccination in adults with HIV-1. *Lancet Infect Dis* 2012;12:966–76.
- Wise J. Covid-19: UK will offer third vaccine dose to severely immunosuppressed people. *BMJ* 2021;374:n2160.
- Woldemeskel BA, Karaba AH, Garliss CC, Beck EJ, Wang KH, Laeyendecker O, et al. The BNT162b2 mRNA vaccine elicits robust humoral and cellular immune responses in people living with HIV. *Clin Infect Dis* 2021:1268–70.
- World Health Organization, Coronavirus (COVID-19) Dashboard WHO Coronavirus (COVID-19) Dashboard with Vaccination Data. <https://covid19who.int/>, 2022 (accessed 31 March 2022).
- Zeng G, Xu L, Feng S, Tang J, Wang X, Li G, et al. IgG antibody responses and immune persistence of two doses of BBIBP-CorV vaccine or CoronaVac vaccine in people living with HIV (PLWH) in Shenzhen, China. *Vaccines (Basel)* 2022;10:880.
- Zhang W, Sun H, Atiqzaman M, Sou J, Anis AH, Cooper C. Influenza vaccination for HIV-positive people: systematic review and network meta-analysis. *Vaccine* 2018;36:4077–86.
- Zou S, Wu M, Ming F, Wu S, Guo W, Marley G, et al. Immune response and safety to inactivated COVID-19 vaccine: a comparison between people living with HIV and HIV-naive individuals. *AIDS Res Ther* 2022;19:33.