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COVID-19 vaccine effectiveness among people living with and without HIV in South Carolina, USA: protocol of a population-based cohort study

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ABSTRACT

Introduction Despite the effectiveness of COVID-19 vaccines in preventing severe COVID-19 outcomes, a small percentage of fully vaccinated persons will develop symptomatic or asymptomatic infections with SARS-CoV-2, which is referred to as 'breakthrough COVID-19'. People living with HIV (PLWH) appear to have an elevated risk of severe COVID-19 outcomes, yet the effectiveness of the COVID-19 vaccine in this population remains unclear due to the limited research efforts in this population in the real world. This study aims to characterise and compare the breakthrough COVID-19 (eg, prevalence and disease severity) between PLWH and non-PLWH and then examine whether HIV markers play a role in COVID-19 vaccine effectiveness within the PLWH population.

Methods and analysis This cohort study will merge electronic health records data from multiple data sources in South Carolina (SC), including the 'HIV Cohort' (n=12 203) identified from the statewide Enhanced HIV/AIDS Reporting System, 'Vaccine Cohort' from the Statewide Immunisation Online Network which provides patient-level immunisation records (n=~1.71 million), and 'COVID-19 Cohort' which includes healthcare encounters and COVID-19 diagnosis information for all individuals who were tested for COVID-19 (n=~3.41 million). The PLWH will be matched with a comparison group of non-PLWH by the propensity score matching method. To distinguish the role of immunity level in affecting the vaccine effectiveness, we will conduct subgroup analyses to compare the outcome of virally controlled and immunosuppressed PLWH with non-PLWH. Conditional logistic regression and generalised linear models will be employed to analyse the relationship between HIV status and protection durability by adjusting for potential confounders.

Ethics and dissemination The study was approved by the Institutional Review Board at the University of South Carolina (Pro00117583) as a Non-Human Subject study. The study's findings will be published in peer-reviewed journals and disseminated at national and international conferences and through social media.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ The data integration from multiple data sources to form cohort analyses will enable a robust evaluation of vaccine effectiveness via monitoring COVID-19 breakthrough infections by using a large representative sample with a long follow-up.

⇒ This large-scale population-based cohort study allows for applying a propensity score matching design to match people living with HIV (PLWH) with their non-PLWH counterparts.

⇒ Results from this proposed study will add to a limited body of evidence by examining a broad clinical spectrum of COVID-19 breakthrough infections (rather than only hospitalised breakthrough infections) and explore the potential variances of clinical spectrum in different hosts (PLWH and non-PLWH).

⇒ Some lab markers (eg, neutralising antibody) are not available in the merged data sources, which may need caution when interpreting the vaccine effectiveness results.

INTRODUCTION

The COVID-19 pandemic is expected to continuously impose enormous burdens of morbidity and mortality while severely disrupting societies and economies worldwide. Effective and durable SARS-CoV-2 vaccines hold the potential to dramatically alter the COVID-19 pandemic.[1 2] Remarkable achievements of COVID-19 vaccine development were observed in large, randomised controlled trials,[3 4] where several vaccines were found to be safe and efficacious in preventing symptomatic COVID-19. Despite the high level of vaccine effectiveness, a small percentage of fully vaccinated persons (ie, received all recommended doses of an FDA-authorised COVID-19 vaccine) will develop symptomatic or asymptomatic infections with SARS-CoV-2,[5] which is referred to as COVID-19 vaccine breakthrough cases (hereafter as 'breakthrough COVID-19'). According to national surveillance data,[5] 27% of breakthrough COVID-19 were asymptomatic, 10% of patients were hospitalised and 2% of patients died. As of 23 August 2021,

a total of 11 050 breakthrough infections were reported as hospitalised or dead across the USA.[6] Understanding the COVID-19 vaccine effectiveness in real-world settings is critical to monitoring the disease and preventing the resurgence of COVID-19 cases, especially among immunocompromised populations such as people living with HIV (PLWH).

PLWH appear to be at elevated risks of COVID-related illness, hospitalisation and death.[7] Thus, ensuring the effectiveness of COVID-19 vaccine in PLWH is pressing. However, data on the effectiveness of COVID-19 vaccine among PLWH remain limited because PLWH were not representatively included in the initial effectiveness trials[8] and did not account for a large proportion in the existing efforts to investigate COVID-19 vaccine effectiveness among immunocompromised populations in the real world. PLWH experience the acquired immunodeficiency caused by HIV and could induce progressive CD4 T cell depletion.[9] Reduced CD4 counts correlate with reduced concentrations of antibodies to SARS-CoV-2.[10] A growing body of evidence suggests that, compared with non-PLWH, PLWH may mount similar humoral immune responses to COVID-19 vaccines,[11–15] but mixed results were observed when it relates to different immunosuppression levels.[16 17] A less rigorous response to COVID-19 vaccination in PLWH could be explained by the CD4 depletion,[18] uncontrolled viral load[19] and the disease severity phases.[20] The quick decline in antibody levels may lead to a higher susceptibility to breakthrough infections. This raises global concerns regarding how long the protective antibodies can last and function effectively post-COVID-19 vaccination. However, the existing comparisons of the COVID-19 vaccine effectiveness between PLWH and non-PLWH are largely based on case reports or case series. The more robust evidence from real-world data of large, population-level based cohorts is warranted.

The increasing availability of electronic health records (EHRs) has presented the opportunity to discover new knowledge via extensive data linkage and integration. Since 1986, the South Carolina (SC) Department of Health and Environmental Control (DHEC) has been collecting the statewide EHR of HIV diagnosis, risk factors and laboratory tests via the Enhanced HIV/AIDS Reporting System (e-HARS), a statewide confidential name-based reporting of HIV/AIDS.[21 22] Since the outbreak of COVID-19 pandemic, several other statewide data sources (South Carolina Statewide Immunisation Online Network (SIMON), South Carolina COVID-19 Cohort (S3C)), has been established. Specifically, SIMON includes all record of COVID-19 vaccination information and S3C includes healthcare encounter and COVID-19 diagnosis information of all SC residents who were tested for COVID-19.

Based on our ongoing project,[23] we already established a 'HIV cohort', which consists of a total of 12 203 PLWH who were diagnosed with HIV during 2005–2020 in SC. To conduct the proposed study, we will continue work with SC Revenue and Fiscal Affairs Office (RFA), who serve as the honest broker for the data linkage and integration for our ongoing project, to merge the SIMON and the S3C datasets. The HIV and S3C cohorts will be updated through December 2022 to ensure an ample sample size of PLWH and an adequate follow-up observation period to detect the breakthrough cases. With the data integration, the current exploratory study has the following specific aims:

Aim 1
Characterise and compare breakthrough COVID-19 infections (eg, prevalence and disease severity) between PLWH and a propensity score matched non-PLWH comparison group overall and stratified by vaccine product type, different COVID-19 phases (eg, pre-Delta/Omicron variant and post-Delta/Omicron variant) and underlying medical conditions (ie, comorbidities).

Aim 2
Examine whether HIV markers (eg, low CD4 counts, detectable viral load, clinical AIDS stage), and HIV treatment (antiretroviral therapy (ART)) play a role in COVID-19 vaccine effectiveness within the PLWH population.

Our study would complement existing studies and provide robust real-world evidence regarding the vaccine effectiveness against COVID-19 and breakthrough infections among PLWH. The findings from the proposed study are essential to promoting health equity between PLWH and non-PLWH and better informing clinical management and guidelines on future vaccination distribution strategies. Characterisation of COVID-19 breakthrough infections in the vulnerable groups of PLWH may help to develop guidance to augment their protection, either by continued social distancing, or by additional active or passive vaccinations (eg, provide neutralising antibodies, vaccine boosters or long acting monoclonals). Exploring the impact of different immunosuppression levels (eg, CD4 counts, viral load) in affecting vaccine effectiveness could help to understand the benefit of additional preventive measures for more vulnerable PLWH (eg, those with low CD4 counts) and prevent the resurgence of COVID-19 cases.

METHODS AND ANALYSIS
Overview of the study design
Given the complexity of data sources, we propose a conceptual framework to guide our proposed research. As shown in figure 1, we will first merge databases from different data sources (eg, HIV cohort, SIMON, S3C) for the data preparation of this study. Then the vaccinated PLWH and a comparison group of vaccinated non-PLWH will be identified from the merged database via propensity score matching (PSM). After the target populations are matched, the COVID-19 vaccine effectiveness in PLWH and non-PLWH will be
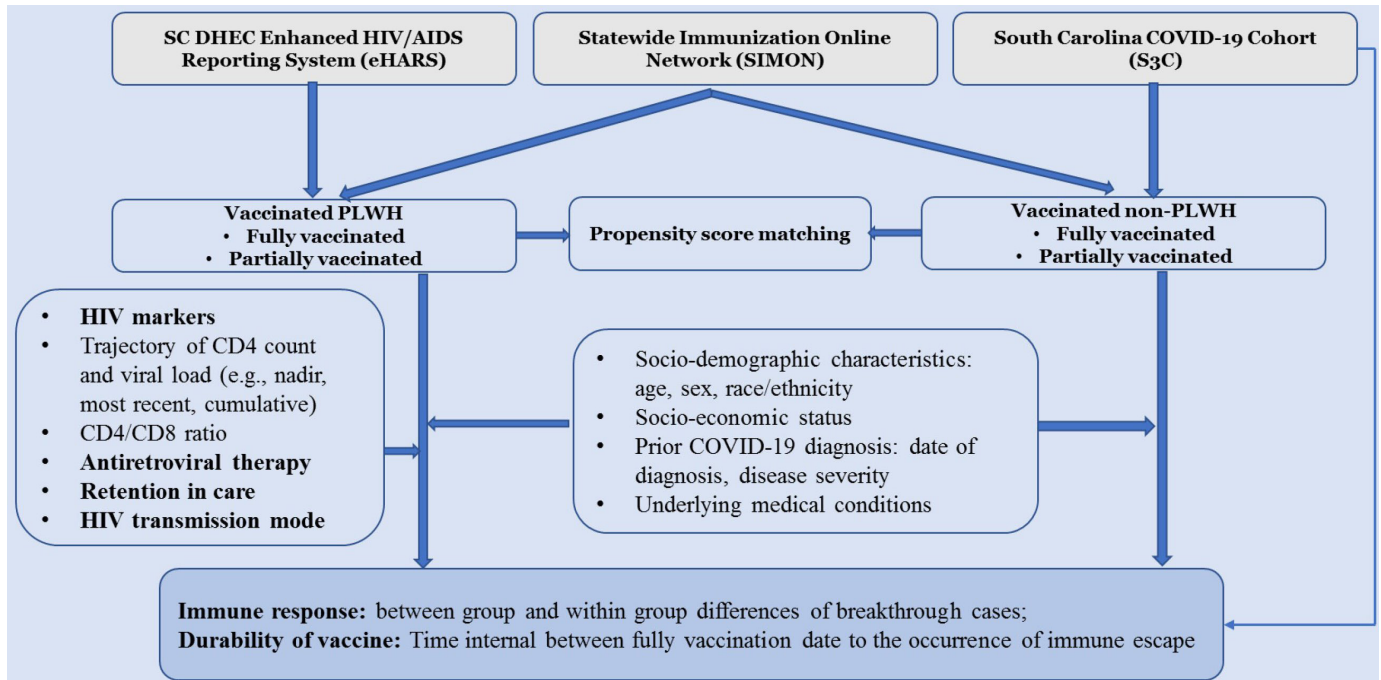
Figure 1 Conceptual framework. DHEC, Department of Health and Environmental Control; PLWH, people living with HIV; SC, South Carolina.

examined via percentage of and time to the occurrence of breakthrough infections. Guided by the conceptual framework, we will obtain a comprehensive view of the COVID-19 vaccine effectiveness among PLWH and non-PLWH. Within the PLWH population, we will also investigate whether HIV markers (eg, low CD4 counts, uncontrolled viral suppression, AIDS stage), and HIV treatment (ART) play a role in COVID-19 vaccine effectiveness. The potential confounders that might compound these effects include socioeconomic status (SES), prior COVID-19 diagnosis (eg, date of diagnosis, COVID-19 disease severity), local county-level COVID-19 incidence and retention in care status (for within PLWH group analysis).

Data sources
HIV cohort data
Since 2017, our research team have been using a Big Data approach to examine treatment gaps among 12 203 PLWH who were diagnosed with HIV during 2005–2020 in SC, with follow-up record until 2021. The study population of this project includes all PLWH who were ≥18 years at HIV diagnosis in SC. In our ongoing project, around 15 years (2005–2020) of healthcare encounter data are extracted from longitudinal EHR from a variety of state agencies (figure 2). Details of the SC eHARS information have been described elsewhere.[23] Briefly, the individual variables we will derive from SC eHARS include date of HIV diagnosis, sociodemographic (eg, age, race/ethnicity, risk exposure (men who have sex with men (MSM), drug user), CD4 count and viral load). This HIV cohort will be updated through at least December 2022.

Vaccination data
The COVID-19 vaccination record since 2021 (2 January 2021–14 March 2022 so far) will be extracted from the SIMON in SC DHEC—a new Immunisation Information System used to house information on person level allocations of vaccine doses. SIMON allows for gathering and analysis of real-time or near-real-time vaccination data in vaccination clinics. SIMON is compatible with all web browsers and devices and meets the requirement for stage 3 meaningful use of the EHR incentive programme by the Centers for Medicare & Medicaid Services.[24] It will also generate provider-level immunisation coverage reports for quality improvement efforts. SIMON supports the SC Entire Immunisation Partner Community, which includes private clinics, school nurses, local public health agencies and vaccines for children (VFC) providers, and the vendors. The features of this new system (replacing the old South Carolina Immunisation Registry) include brand-new data quality measures which ensure a more reliable system is maintained; the upgraded reporting capabilities for clinicians including provider site, region and population characteristics; enhanced electronic exchange with the EHR systems including forecast feature; and the vaccine deduplication features that help consolidate records from multiple providers into a single record for each patient.

COVID-19 cohort data
Since the outbreak of COVID-19, we established the S3C[25] on 06/2020 using integrated patients' EHR data from eight state-level data sources which includes 1-year pre-COVID healthcare utilisation data for all the individuals. The S3C
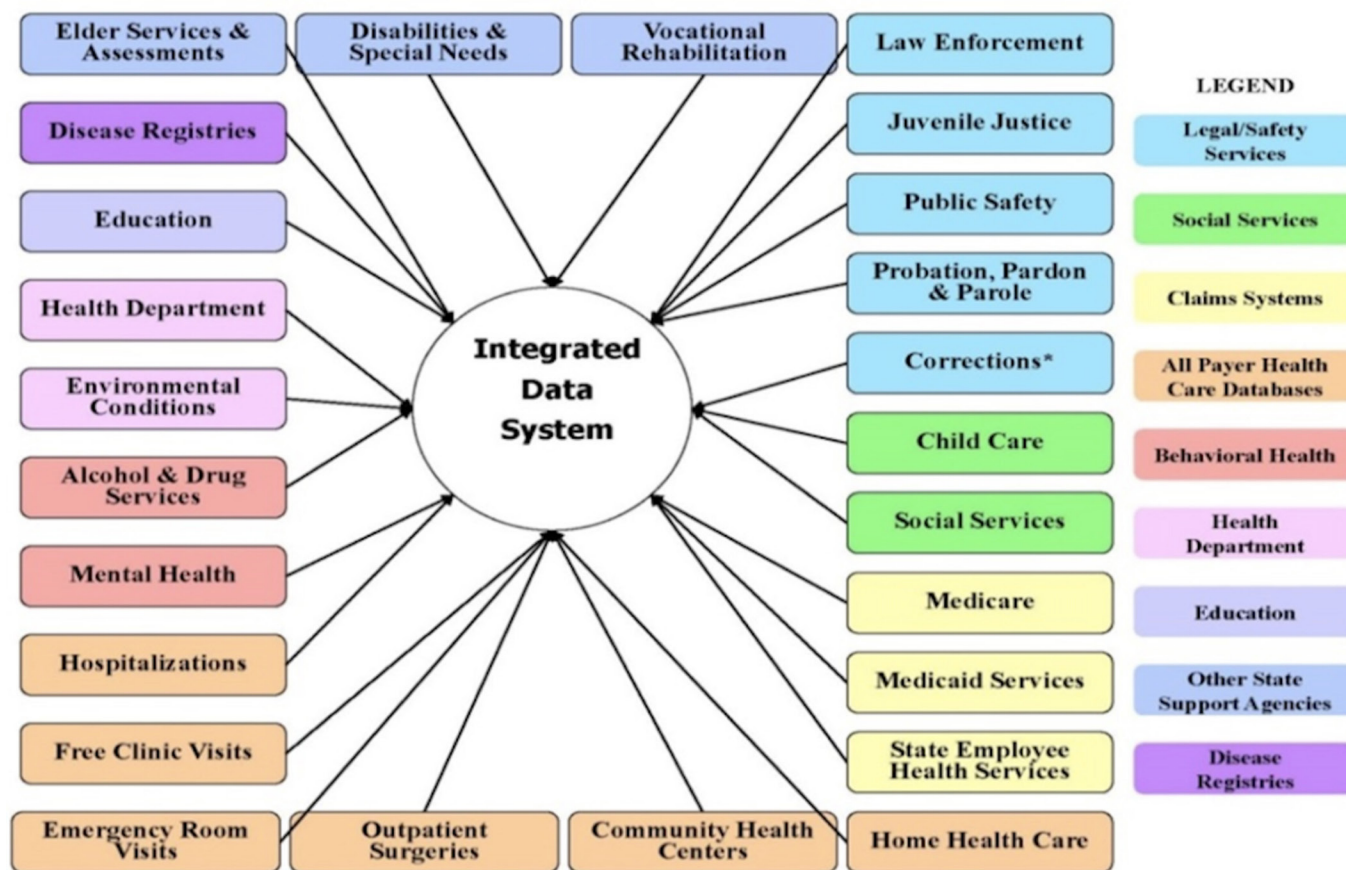
Figure 2 SC state data warehouse. SC, South Carolina.

cohort will be updated through at least December 2022. The statewide record of COVID-19 testers is included in this cohort, which consists of both COVID-19 positive and negative individuals. SC Law (44-29-10) and Regulations (61-20) require mandatory reporting of COVID-19 diagnosis to DHEC. The COVID-19 positive cases are defined based on the SC statewide case report form (CRF) ('Human Infection with 2019 Novel Coronavirus 'CRF') for COVID-19 infection issued by SC DHEC. The CRF contains information about lab-confirmed and probable cases of COVID-19, including the case classification and identification, hospitalisation, intensive care unit (ICU) and death information, case demographics, clinical course, symptoms, medical history and social history.

Data linkage and integration

The SC RFA will serve as the honest broker for the linkage of all data and remove the identifiable information from the linked data before releasing it to the research team. Various data resources will be integrated through the following steps. First, the HIV Cohort will be updated from SC DHEC. Second, RFA will link HIV cohort to SIMON and S3C. RFA has agreed to follow the established procedure to update data through 2022 and also link the existing HIV and COVID-19 databases to the vaccine immunisation database. The RFA's deidentified system-generated ID number ensures confidentiality but

allows the study team to conduct data mining at both the individual and aggregated data levels. For data security, only the final, deidentified dataset will be released to investigators for analysis. After the data release to our research team, we will assess the data quality related to missing, aberrant or extreme values.

Measurement of key study variables

COVID-19 breakthrough

A vaccine breakthrough infection is defined as the detection of SARS-CoV-2 RNA or antigen in a respiratory specimen collected from a person ≥14 days after receipt of all recommended doses of an U.S. Food and Drug Administration (FDA)-authorised COVID-19 vaccine.[6]

Vaccination status

Vaccine information included dates and location of vaccination, and vaccine product will be ascertained through pulling records from SIMON database in SC. Sources of documentation include vaccination cards, hospital records and state vaccine registries which will be searched once or twice depending on the vaccine product.

Vaccine doses will be classified as administered if source documentation is identified. For mRNA vaccines (Pfizer-BioNTech or Moderna), they are administered as a two-dose series. The interval between doses is 21 days for Pfizer-BioNTech and 28 days for Moderna. The Janssen

(Johnson &Johnson) COVID-19 vaccine, which was recently introduced following its Emergency Use Authorisation in February 2021,[26] is a single-dose vaccine. The homologous or heterologous booster dose administered at least 6 months after completion of primary vaccination will also be considered.[27] Vaccination status will be classified based on the number of vaccine doses received before a reference date, which will be either the date of symptom onset for COVID-19 breakthrough or the end date of this project for individuals without COVID-19 breakthrough. Individuals will be classified as: partially vaccinated if they receive one dose of Pfizer-BioNTech or Moderna vaccines ≥14 days before the reference date; fully vaccinated if they received either two doses of Pfizer-BioNTech or Moderna vaccines or a single dose of Janssen ≥14 days before the reference date; and boosted vaccination if they receive the booster dose. Some individuals will also be defined as mixed-dose series if they take two different types of vaccine products. As protective immunity from COVID-19 vaccines is not expected immediately after the first dose,[28] patients who received a first dose <14 days before the reference date will be excluded from the analysis. Patients who received a COVID-19 vaccine that had not been authorised in the USA will be excluded as well.

Identification of COVID-19 breakthrough

COVID-19 breakthrough will be identified from the S3C database, which documents the diagnosis history of COVID-19. EHR after at least 14 days of vaccination will be retrieved from the S3C database to identify the COVID-19 diagnosis. The criteria of case ascertainment were described in the standardised surveillance case definition of COVID-19.[29] Clinical course information include symptom category during onset of illness (ie, symptomatic, asymptomatic, unknown), and development of pneumonia and acute respiratory distress syndrome (ARDS). For symptomatic patients, the CRF documented specific symptoms that were experienced during the illness, such as fever, olfactory and taste disorders, and difficulty breathing. The percentage of COVID-19 breakthrough and protection durability (ie, time interval from full vaccination to the occurrence of COVID-19 breakthrough or to the end date of the study period, whichever earlier) will be calculated to reflect the vaccine effectiveness.

Severity of COVID-19 breakthrough

Based on WHO criteria,[30] we will place the breakthrough infections into strata: 'mild' (outpatient, WHO severity 1–3), 'moderate' (hospitalised without invasive ventilation, WHO severity 4–6), 'severe' (hospitalised with invasive ventilation or extracorporeal membrane oxygenation (ECMO), WHO severity 7–9) and 'mortality/hospice' (hospital mortality or discharge to hospice, WHO severity 10). Using CRF form, DHEC collects information on symptoms of COVID-19 cases. Each symptom had three responses, that is, 'yes', 'no', 'unknown'. Specifically, COVID-19 patients with no symptoms will be categorised

as asymptomatic; individuals who have any of the various mild signs and symptoms of COVID-19 (eg, fever, cough, sore throat and malaise) will be categorised as mild; whereas COVID-19 patients with difficulty breathing or who developed pneumonia or ARDS will be categorised as moderate. In the CRF, hospitalisation was measured with one question, that is, 'Was the patient hospitalised?' with the responses categorised as 'yes', 'no' and 'unknown'. Patients who were hospitalised and also received mechanical ventilation (or intubation or ECMO) will be categorised as severe. The time interval from symptom onset to hospital admission will also be measured as a secondary clinical outcome. Death was measured using the question 'Did the patient die as a result of this illness?', with the response categories of 'yes', 'no' and 'unknown'. Patients with the response of 'yes' indicate death and otherwise indicate alive. The data sources for each variable are listed in table 1.

Potential confounders

Most of the potential confounders will be extracted from the HIV cohort and include: (1) Individual's characteristics: SES, comorbidities and HIV transmission mode (only applies to PLWH). Comorbidities, such as cardiovascular disease, diabetes mellitus or respiratory disease, will be defined based on the International Classification Diseases (ICD) codes in the updated Charlson Comorbidity Index (CCI) scoring instrument.[31] We will also calculate the cumulative comorbidity burden with CCI score. (2) HIV and other disease-related characteristics: duration of HIV diagnosis, clinical AIDS diagnosis, CD4 counts (initial/nadir/most recent CD4 counts), viral load (initial/peak/most recent viral load) and other immunocompromised conditions, such as solid organ transplant recipients or cancer patients. The CD4 count will be categorised into <200 cells/mm^3, 200–500 cells/mm^3 and >500 cells/mm^3. HIV viral load will be classified into: <200 copies/ml (virally suppressed) and ≥200 copies/mL (virally unsuppressed). (3) COVID-19 diagnosis before vaccination and local COVID-19 epidemic: date of COVID-19 diagnosis, clinical symptoms of COVID-19 infection, disease severity; the publicly available county-level COVID-19 incidence will be mapped at individual level via county code; (4) Substance use: tobacco use, alcohol use and other illicit drug use. (5) Healthcare access and utilisation: type and frequency of healthcare facility visits and HIV retention in care. The types of healthcare services, such as emergency room, inpatient or outpatient visit services in record that the patients received will be obtained. For PLWH, we will define retention in care variable. We first will define 'in HIV care' that refers to having either two or more CD4 or viral load measurements, separated by at least 3 months within a follow-up year. Patients will be considered either in HIV care (coded as 1) or not in HIV Care (coded as 0) each year. Then the proportion of retention in care will be calculated as the sum of years in HIV care divided by the total follow-up years.

Table 1 Multilevel variables and data sources

Data sources	Variables
Statewide Immunisation Online Network	Vaccination status: dates and location of vaccination, vaccine products (Pfizer-BioNTech, Moderna, Janssen/J&J), vaccine doses
SC DHEC Enhanced HIV/AIDS Reporting System	HIV-related information: date of HIV diagnosis, AIDS stage, CD4 counts, viral load, HIV transmission mode Healthcare access and utilisation: geospatial distance to healthcare facility, retention in care
SC Revenue and Fiscal Affairs Office	► Sociodemographics: age, gender, race, ethnicity, residential status (urban/rural) ► Underlying medical conditions: using ICD codes to define a wide range of comorbidities
South Carolina COVID-19 Cohort	COVID-19 diagnosis information from case report form: ► Clinical course: date of COVID-19 diagnosis, diagnosis status (confirmed or probable cases), date of symptom onset, pneumonia, acute respiratory distress syndrome, mechanical ventilation/intubation, ECMO, hospitalisation, intensive care unit and death information ► Symptoms: fever, chill, myalgia, olfactory and taste disorder, shortness of breath, nausea or vomiting ► Medical history/risk behaviours: diabetes mellitus, hypertension, obesity, cardiovascular disease, chronic renal disease, current/former smoker, substance abuse/misuse ► Case demographics: age, sex, state/county of residence, sex, ethnicity, race. ► Aggregated county-level local COVID-19 incidence

DHEC, Department of Health and Environmental Control; ECMO, Extracorporeal Membrane Oxygenation; ICD, International Classification Diseases; SC, South Carolina.

Statistical analysis

Preliminary analysis and PSM

In our preliminary analysis, the iteration of the dataset included around 3.41 million individuals who received any COVID-19 testing prior to October 2021, among whom around 691 083 were adults (≥18 years of age) ever diagnosed with COVID-19 and 6297 living with HIV. Assuming that 35% PLWH would be vaccinated and 6% of vaccinated PLWH would have COVID-19 breakthrough (based on the crude analysis of COVID-19 patient registrar data from Medical University of South Carolina), we anticipate that we would be able to retrieve at least 130 and 50 000 COVID-19 breakthroughs among PLWH and non-PLWH, respectively. This number will continue to expand as our dataset will be updated on a regular basis. To strengthen the causal inference, we propose to use PSM to match PLWH with non-PLWH as a quasi-experimental approach for observational data, which could minimise the selection bias by balancing the baseline sociodemographic characteristics of the two groups and isolate the effect of HIV infection on the outcomes. We will perform 1:1 and 1:2 matching for key sociodemographic variables, such as age, sex and race/ethnicity using nearest neighbour algorithms with a calliper width of 0.1 pooled SD. To test the matching performance, the standardised mean difference (SMD) will be used as one balance diagnostic technique to examine the balance of sociodemographic distribution between PLWH and non-PLWH groups.

Examine the vaccine effectiveness between PLWH and non-PLWH

We will first estimate the percentage and severity (hospitalised or death) of COVID-19 breakthrough in the overall vaccinated individuals and across different subgroups (PLWH vs non-PLWH). To assess the sociodemographic distribution properties of patients with and without COVID-19 breakthrough overall and across different populations (PLWH and non-PLWH), categorical variables will be compared using χ^2 and Fisher's exact tests, and continuous variables will be compared using independent samples t-test or Mann-Whitney test as appropriate.

To investigate whether PLWH are more likely to have COVID-19 breakthrough, in the unmatched analysis, both unadjusted and adjusted ORs will be calculated with (multivariable) logistic/multinomial logistic regressions accounting for potential confounders listed in table 1, such as vaccine types, prior COVID-19 diagnosis, and number of comorbidities (eg, cardiovascular disease) or the cumulative comorbidity burden (CCI score) and the local COVID-19 incidence. Regarding protection durability of COVID-19 vaccine, the generalised linear models will be employed to analyse the relationship between HIV status and protection durability by adjusting for similar potential confounders. To account for the temporal differences in vaccine roll-out and availability on the outcome, the segment regression analysis will also be used across different time windows (eg, Pfizer or Moderna vaccine roll-out time). To investigate the impact of HIV on vaccine effectiveness, we conduct the regression models based on the PSM matched data. To distinguish the role of immunity level in affecting the vaccine effectiveness, we will conduct similar analysis between virally controlled and immunosuppressed PLWH with non-PLWH. In addition, several subset analyses will be conducted, including the subgroups stratified by COVID-19 vaccine product (Pfizer-BioNTech or Moderna or Janssen) or subgroup with geospatial data, which allows us to assess the impact of local COVID-19 incidence on the outcomes. The appropriateness of the adjusting variables will be determined via

the stepwise variable selection and the appropriateness of the interaction will be determined via the likelihood ratio test. If interaction is significant, stratified modelling will be further assessed. The final model will be determined through the Akaike information criterion. The statistical testing hypotheses of interest will be assessed by the Wald test. The estimated coefficient/ORs and their 95% CIs will be reported. All analyses will be performed with SAS (V.9.4) and R software (V.3.6.2).

COVID-19 breakthrough among PLWH

In PLWH group, assessments will be performed to examine the impact of host-specific factors, such as clinical AIDS diagnosis, and different level of HIV markers (eg, CD4 count, viral load) on the breakthrough infections. Besides the common confounders identified in the measurement section, the healthcare access (eg, the type of healthcare facility) and HIV care continuum (eg, retention in care) measures will be adjusted as well in a subgroup analysis when the zip-code geospatial variables are available. Several other subgroup analyses will also be conducted in the premise of ample sample size and considerable prevalence. The logistic regression, multinomial logistic regression and generalised linear mixed model will be applied as appropriate and most optimal models will be determined.

Sensitivity analysis

To enhance the robustness of the findings, several sensitivity analyses will be conducted to test key design features. The first one is the source of COVID-19 vaccine information. Patients in the record will be considered vaccinated if they had source verification of vaccine receipt or a plausible date and location of vaccine receipt. Individuals who received vaccination without source verification, received mixed products of COVID-19 vaccines or partial vaccination will be excluded for sensitivity analysis. Second, the impact of missing information in the predictors will be examined using the complete data analysis or entire cohort with missingness as a category. Similar analytical strategies as in the main analysis will be conducted to check whether these sensitivity analyses will yield similar findings.

Patient and public involvement

None.

ETHICS AND DISSEMINATION

The study was approved by the Institutional Review Boards at the University of South Carolina (Pro00117583) as a Non-Human Subject study. Understanding the COVID-19 vaccine effectiveness among PLWH and non-PLWH is essential to support informed vaccination decision-making in clinical practice. Characterising PLWH who are at a higher risk of COVID-19 breakthrough (low CD4 counts, detectable viral load) may help to inform tailored vaccination strategies against COVID-19 based on HIV markers and develop guidance to augment their protection against risk of COVID-19. Such findings could also help to understand the benefit of additional preventive measures, such as vaccine boosters, for the subgroups of PLWH who are more vulnerable for COVID-19 breakthrough and contribute to the development of preventive and therapeutic agents.

We will publish the findings in peer-reviewed scientific journals and present the study findings at national and international professional conferences and through appropriate social media outlets. We will capitalise on social media and professional networks that can increase the reach and accessibility of findings, such as open access publication, webinars, files and videos available on websites and publicly available channels (eg, YouTube), to increase visibility and impact of the scientific publications and presentations. The dissemination efforts of this project will extend beyond the scientific arena and also target our stakeholders in healthcare system and policy makers in the USA at local (SC DHEC, Prisma Health) and national levels (Centers for Disease Control and Prevention (CDC)) through various policy forums, policy papers and special presentations. We hope that the anticipated success of the proposed project will prompt policy changes in COVID-19 prevention, treatment and care among PLWH in the USA.

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