Preventive Medicine Reports 36 (2023) 102448

Contents lists available at ScienceDirect

Preventive Medicine Reports

journal homepage: www.elsevier.com/locate/pmedr

Time-to-completion of COVID-19 vaccination primary series varies by HIV viral load status among people who inject drugs in Baltimore, Maryland

Pieter Baker [a,b,*], Javier A Cepeda [a], Catherine Schluth [a], Jacquie Astemborski [a], Kenneth A. Feder [c], Jacqueline Rudolph [a], Jing Sun [a], Gregory D. Kirk [a,d], Shruti H. Mehta [a], Becky L. Genberg [a]

[a] Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, United States
[b] Department of Epidemiology & Biostatistics, Arnold School of Public Health, University of South Carolina, Columbia, United States
[c] Department of Mental Health, Johns Hopkins Bloomberg School of Public Health, Baltimore, United States
[d] School of Medicine, Johns Hopkins University, Baltimore, United States

ARTICLE INFO

Keywords:
COVID-19
SARS-CoV-2
Vaccine uptake
Injection drug use
ART adherence
Viral suppression

ABSTRACT

People who inject drugs (PWID) may have diminished access to essential preventive services like COVID-19 vaccination given structural and substance use barriers. We aimed to assess the role of HIV on COVID-19 vaccination uptake among adult PWID participating in the ALIVE cohort study in Baltimore, Maryland who were alive as of April 2021. We abstracted COVID-19 vaccination data from electronic medical records via the regional health information exchange. We used Kaplan-Meier method to estimate time from universal vaccine eligibility (April 6, 2021) to completion of the COVID-19 vaccination primary series (1 dose J&J or 2 doses mRNA) by HIV viral load status (uninfected, PWH [HIV-RNA < 400 copies/mL], PWH [HIV-RNA ≥ 400 copies/mL]) and Cox Proportional Hazards regression to adjust for potential confounders. Our sample (N = 960) was primarily black (77%) and male (65%) with 31% reporting recent injection drug use. Among 265 (27%) people living with HIV (PWH) in our sample, 84% were virally suppressed. As of February 22, 2022, 539 (56%) completed the primary series, 131 (14%) received a single dose of mRNA vaccine and 290 (30%) remained unvaccinated. Compared to PWID without HIV, virally suppressed PWH were more likely to complete the primary series (Adjusted Hazard Ratio [aHR]:1.23,95% Confidence Interval [95 %CI]:1.07,1.50), while PWH who were not virally suppressed were less likely (aHR:0.72,95 %CI:0.45,1.16), although this was not statistically significant. We conclude that among PWID, HIV infection and viral suppression is associated with quicker vaccination uptake, likely due to HIV care engagement. Targeted improvements along the HIV care continuum may bolster vaccine uptake.

1. Introduction

COVID-19 vaccination remains a key strategy for preventing severe complications resulting from SARS-CoV2 infection. The COVID-19 vaccines are safe and effective, including for people living with HIV (PWH) (Plummer and Pavia, 2021), and vaccine uptake is critically important for vulnerable populations such as PWH (Hiv, 2021) and people who inject drugs (PWID). PWH who are immunocompromised are more likely to have underlying co-morbidities placing them at higher risk for COVID-19 related morbidity and mortality. (Mohammed et al., 2020; Childs et al., 2020; Nomah et al., 2021) Prior to COVID-19 vaccine availability, HIV had been associated with higher risk of SARS-CoV-2 infection, severe outcomes, and an estimated 80% excess risk of death following infection compared to those without HIV (Ssentongo et al., 2021; Yang et al., 2021). Viral suppression is significant as differences in risk of severe outcomes following COVID-19 infection (i.e. hospitalization, tachypnoea, hypoxaemia, asphyxia, hyperventilation, or death) are higher among PWH with detectable viral load, than PWH with undetectable viral load. (Nomah et al., 2021).

Injection drug use (IDU) is also associated with an increased number of co-morbidities (Degenhardt et al., 2017; Csete et al., 2016; Sun et al., 2022; Ao et al., 2022) and opioid use has been associated with higher odds of mortality and ICU admission for COVID-19, compared to those who do not use opioids. (Ao et al., 2022) PWID may face additional

* Corresponding author.
E-mail address: pieter@mailbox.sc.edu (P. Baker).

https://doi.org/10.1016/j.pmedr.2023.102448
Received 30 March 2023; Received in revised form 30 August 2023; Accepted 27 September 2023
Available online 28 September 2023

barriers to COVID-19 vaccine uptake due to social/economic disadvantages, residential and transportation instability, criminal justice involvement, structural barriers, stigma, and related discrimination. (Dunlop et al., 2020) PWID living with HIV may have fewer barriers to timely vaccination due to their engagement with HIV care and services, although HIV viral suppression may have been impacted by disruptions in HIV treatment due to the pandemic. (Dunlop et al., 2020) In prior research among PWH, self-reported viral suppression was associated with self-reported receipt of at least one dose of the COVID-19 vaccine. (Jaiswal et al., 2022) However, it remains unclear how viral suppression relates to completion of the primary series, and whether there was slower uptake of vaccination by viral load status after accounting for substance use and other factors that may delay engagement in care and services in this population. Viral suppression and routine connection to HIV care may also provide opportunities to engage with providers regarding other health concerns such as chronic conditions or recommended vaccinations. If HIV-positive PWID with unsuppressed viral load were slower to complete COVID-19 vaccination than PWID who were virally suppressed or uninfected with HIV, this would indicate that additional efforts may be needed to engage this difficult-to-reach population.

There are limitations to existing studies of vaccine uptake in vulnerable populations. To date, the majority of research surrounding COVID-19 vaccination, among PWID in particular, has examined participant hesitancy/willingness and/or self-reported uptake of at least one dose as the primary outcome (Andreas et al., 2022) which has inherent limitations due to recall bias. Understanding how quickly vulnerable populations get vaccinated and factors associated with delays will be important for future vaccine and prevention campaigns. (Mathieu et al., 2021; Prevention CfDCa. COVID Data Tracker. US Department of Health and Human Services. https://covid.cdc.gov/covid-data-tracker. Published, 2022; Dong et al., 2020) This was important during the critical period following the initial vaccine roll-out (December 2020) when community transmission was high while vaccination rates remained relatively low. Since the release of the COVID-19 vaccine, troublesome SARS-CoV-2 variants have emerged alongside recommendations for additional COVID-19 boosters. This has reinforced the need to understand vaccine uptake among key populations.. Other existing research relying on administrative data has not been able to account for important covariates, including socio-structural and substance use behaviors, which may impede vaccination efforts among vulnerable populations. To address this, our approach leverages clinical data from a regional health information exchange linked to detailed participant characteristics (including substance use behaviors) from a longitudinal cohort of PWID.

The objective of this study was to evaluate differences in COVID-19 uptake by HIV viral load status among PWID. We hypothesized that among PWID, PWH with lower viral loads (<400 copies/ μL) would have faster time-to-completion of the primary series than PWH with higher viral loads (≥400 copiess/ μL) and those not infected with HIV, after controlling for key sociodemographic, health status, and drug use variables.

2. Methods

2.1. Study population and data collection

Our study population consisted of participants enrolled in the ALIVE Study, which has been described in detail elsewhere (Vlahov et al., 1991), who were alive as of April 6, 2021. Briefly, ALIVE is a prospective community-based cohort study that follows adults (aged 18 years or older) in or near Baltimore, Maryland, with a history of injection drug use. At biannual study visits, detailed data on participant characteristics, substance use behaviors, and health status are collected via interviewer-administered surveys. Blood samples are collected and tested for HIV and Hepatitis C virus (HCV) antibodies and viral load. The research was granted ethical approval by the Institutional Review Board at Johns Hopkins University and all participants provided written informed consent before participating. In this analysis, we used data on participant characteristics, health status, and substance use behaviors collected from the last ALIVE study visit prior to March 2020. We selected April 6, 2021 as the time origin for our analysis because this is the date when Maryland entered Phase 3 of the COVID-19 vaccination roll-out and the entire general population (16 years and older) was considered eligible for vaccination. Among participants included in this analysis, the median time between last ALIVE study visit and the origin (April 6, 2021) is 538 days, with an interquartile range of 162 days.

COVID-19 vaccination status was determined using electronic records in the Chesapeake Regional Information System for our Patients (CRISP) health information exchange. CRISP compiles electronic medical record data and information on clinical encounters with nearly all participating providers throughout the region (Maryland, Washington DC, West Virginia), as well as records from the Maryland Department of Health's vaccine surveillance system. We performed identity matches using the CRISP platform's probabilistic matching algorithm with name and date of birth data from the ALIVE study. Eligibility included all ALIVE participants with linked identities in CRISP (n = 960) who were alive as of April 6, 2021. Mortality ascertainment in ALIVE includes annual linkage to vital status data from the National Death Index (NDI) with confirmation from state death certificates. To exclude those that died prior to the analysis timeframe or were censored during the study period, we queried data from the 2020 and 2021 National Death Index final and early releases, respectively. Trained study staff abstracted information from CRISP on COVID-19 vaccination, including dates of receipt and vaccine manufacturer, as well as COVID-19 diagnoses and dates of infection. We conducted data abstraction between September 28, 2021 and February 22, 2022, looking back in the CRISP database to records since December 2020.

2.2. Primary outcome and measures from CRISP

We defined our outcome as the completion of the COVID-19 primary vaccination series, achieved on the date of receipt of either: 1) one dose of the Johnson & Johnson adenovirus vector vaccine or 2) at least two doses of mRNA vaccine (Pfizer or Moderna). We calculated length of follow-up for each participant by taking the difference in time (in weeks) between the origin (April 6, 2021) and the date of completion of the primary series. Censoring was defined by the date of CRISP data abstraction or date of death (for those who died after the start of the study period, but before vaccination or completion of data abstraction). We also used data abstracted from CRISP to construct a variable for prior COVID-19 infection (confirmed in CRISP before date of vaccination or censoring: yes/no). Eligible ALIVE participants who could not be matched to CRISP (n = 108) or whose vaccine receipt listed "unspecified" (n = 1) were considered to have missing data for the outcome and were thus omitted from the analysis. We also excluded participants who were vaccinated prior to the study origin (n = 158) in our main analysis, but these participants were included in a sensitivity analysis.

2.3. Laboratory measures from ALIVE

Samples collected at the last ALIVE study visit prior to March 2020were used to test for HCV status (laboratory confirmed antibody: positive, negative) and HIV viral load (VL). HIV infection was determined by an enzyme-linked immunoabsorbent assay to detect HIV-1 anitbodies and confirmed via Western blot. We used reverse-transcription PCR methods (Roche Amplicor HIV-1 Monitor Test [limit of detection: 50 copies/μL]) to quantify plasma HIV-1 RNA levels. We constructed our primary exposure of interest, HIV viral load status, as a three-level categorical variable with the following levels: HIV negative, HIV suppressed (VL < 400 copies/μL), and HIV unsuppressed (VL ≥ 400 copies/μL).

2.4. Self-reported measures from ALIVE

We included self-reported sociodemographic, substance use, and health status variables from participants' last ALIVE study visit prior to March 2020. Covariates were selected based on a previously established or hypothesized association with COVID-19 vaccination and HIV viral load. (Wickersham et al., 2022; Viswanath et al., 2021; Valasek et al., 2022; Robinson et al., 2021; Quinn et al., 2020; McCree et al., 2021; Qi et al., 2021; Fulda et al., 2022; Rane et al., 2022; Cepeda et al., 2022) We constructed the sociodemographic variables as follows: age (<50, 50–64, ≥65 years); race (black, not Black); sex (male, female); income (<$5,000/year, ≥$5,000/year); education (≤high school, >high school); currently working (yes, no); and homeless (yes, no). We constructed the self-reported health status and substance use variables from the prior 6 months as follows: chronic lung disease diagnosis (ever; yes, no); recent marijuana use (yes, no); recent injection drug use (yes, no); recent non-injection stimulant use (yes, no); recent non-injection heroin use (yes, no); and smoking (≥1pack/day, <1pack/day).

2.5. Statistical analysis

First, we conducted descriptive statistics and univariate survival analysis using the Kaplan-Meier method to evaluate time between the origin and completion of the primary series for the entire sample and by HIV viral load status. We present an inverse survival curve (1 – Kaplan Meier Estimate) to plot the probability of completing the primary series over time. Then, we used the log-rank test to evaluate differences in median time to vaccination by HIV viral load status (HIV negative, HIV positive [VL < 400 copies/μL], HIV positive [VL > 400 copies/μL]). We also examined (using log rank tests) potential correlates of time-to-completion of the primary series among the sociodemographic, health status, and substance use behavior variables (previous six month). Next, we used Cox Proportional Hazards regression analysis to assess the relationship between HIV viral load and time-to-vaccination while accounting for potential confounders. We report unadjusted hazard ratios for HIV viral load status and all sociodemographic, health status, and substance use variables statistically significant in bivariate survival analysis with a log-rank p-value of less than 0.1. For the adjusted model, we used a stepwise model building approach, introducing factors into the final model that had a significant unadjusted Hazard Ratio at $p < 0.05$, checking for changes in effects, testing for all logical interaction ($p < 0.05$ threshold for testing of interaction terms), and assessing the proportional hazards assumption for each construct included in the final model. All data analyses were conducted using SAS (version 9.4), without adjustment for multiple testing.

To assess completion of the primary series only among those with HIV we conducted a sensitivity analysis on our models with a subsample restricted to PWH. We also conducted a sensitivity analysis to assess our models using an earlier origin of December 12, 2020 to reflect the first date of Phase 1A restricted eligibility in Maryland (compared to our origin of April 6, 2021 which reflected general availability to all adults).

3. Results

3.1. Descriptive statistics and Time-to-Completion of primary series

After omitting participants that died (n = 40) or had been vaccinated (n = 158) prior to the origin (4/6/2021), the analytical sample included 960 ALIVE participants with linked CRISP data. The sample was primarily black (78%), male (67%), and older (50–64 years: 60%; ≥65 years: 14%) with 29% reporting recent IDU. Among the 317 PWH in our sample (28%), most had a HIV viral load less than 400 copies/μL (85%) (Table 1). In our sample, 70% (n = 670/960 were vaccinated with at least 1 dose, 80% of which completed the primary series (n = 539/960, 56% of analytic sample). In total, 421 participants (44%) were censored as they remained unvaccinated (n = 273/960, 28%), received just one

Table 1
Descriptive statistics and median time-to-completion of COVID-19 vaccination primary series by sociodemographic, health status, and substance use variables among people who inject drugs in Baltimore, Maryland (n = 960).

Sociodemographic characteristics	n (%)	Median time-to-completion in weeks (95 %CI)*	p-value†
Age Category	101	8.1 (5.0, 20.9)	<0.0001
≥ 65 years	(10.5)		
50–64 years	581	15.6 (13.1, 20.6)	
	(60.5)		
<50 years	278	–	
	(29.0)		
Race (Black)	735	15.9 (13.3, 21.4)	<0.0001
	(76.6)		
Race (not Black)	225	–	
	(23.4)		
Sex (Female)	333	–	0.0023
	(34.7)		
Sex (Male)	627	20.0 (15.6, 26.0)	
	(65.3)		
Income (≤$5k/month)	669	26.9 (20.4, 34.0)	0.0363
	(72.2)		
Income (≥$5k/month)	257	18.7 (10.3, 25.0)	
	(27.8)		
Education (<High School)	509	25.0 (18.3, 32.4)	0.9204
	(53.1)		
Education (≥High School)	450	24.0 (17.3, 32.0)	
	(46.9)		
Working (Yes)	133	22.1 (13.7, 32.1)	0.4281
	(14.2)		
Working (No)	801	25.0 (18.7, 29.6)	
	(85.8)		
Homeless (Yes)	127	–	0.0075
	(13.6)		
Homeless (No)	810	22.1 (16.3, 26.9)	
	(86.4)		
Health Status Variables			
General Health Status	329	20.0 (14.3, 25.9)	0.4565
Levels 1,2	(35.3)		
Level 3	328	26.9 (17.3, 36.9)	
	(35.1)		
Levels 4,5	276	26.6 (18.4, 36.6)	
	(29.6)		
Prior COVID-19 Infection (Yes)	94 (9.8)	42.1 (15.4, 46.0)	0.1846
Prior COVID-19 Infection (No)	866	23.9 (18.7, 28.0)	
	(90.2)		
HCV Infection (Yes)	734	25.0 (18.9, 30.3	0.8244
	(76.5)		
HCV Infection (No)	225	23.9 (16.1, 37.0)	
	(23.5)		
HIV Infection	695	28.3 (23.9, 40.4)	0.0004
HIV -	(72.4)		
HIV + (VL ≤ 400 copies/	222	12.4 (9.4, 18.4)	
μL)	(23.1)		
HIV + (VL > 400 copies/	43 (4.5)	–	
μL)			
Chronic Lung Disease Dx	218	17.7 (11.4, 28.1)	0.0902
(Yes)	(23.3)		
Chronic Lung Disease Dx	719	25.3 (20.1, 33.1)	
(No)	(76.7)		
Substance Use Behaviors§			
Recent Marijuana (Yes)	184	25.1 (16.0, 39.4)	0.8258
	(19.7)		
Recent Marijuana (No)	749	23.9 (18.9, 28.1)	
	(80.3)		
Recent IDU (Yes)	289	–	<0.0001
	(31.1)		
Recent IDU§ (No)	640	18.3 (13.3, 23.3)	
	(68.9)		
Recent non-IDU stimulant	331	34.9 (26.0, 46.0)	0.0037
(Yes)	(34.5)		
Recent non-IDU stimulant	629	19.0 (15.0, 24.7)	
(No)	(65.5)		
Recent non-IDU Heroin	262	27.2 (21.0, 46.0)	0.1984
(Yes)	(27.3)		

(continued on next page)

Table 1 (*continued*)

Sociodemographic characteristics	n (%)	Median time-to-completion in weeks (95 %CI)*	p-value†
Recent non-IDU Heroin (No)	698 (72.7)	23.1 (17.0, 29.1)	
Smoking (≥1 pack/day)	165 (17.8)	33.1 (19.9, 46.0)	0.0911
Smoking (<1 pack/day)	760 (82.2)	23.3 (17.0, 27.1)	

*If < 50% completed the primary series, median time-to-completion remains undefined (-).
† Log-rank Test.
§Previous six months.

dose of the mRNA vaccine (n = 131/960, 14%), or died during the follow-up period prior to being vaccinated (n = 17/960, 2%) [Fig. 1].

The median time-to-completion of the primary series is our sample was 24.3 weeks (95% Confidence Interval [95 %CI]: 19.9, 28.9 weeks), or, by September 23, 2021. Compared to those uninfected with HIV (28.3 weeks, 95 %CI: 23.9, 40.4), median time-to-vaccination was faster among PWH who were virally suppressed (12.4 weeks, 95 %CI: 9.4, 18.4) but slower among PWH with detectable viral loads (median time undefined as fewer than 50% completed the primary series); log-rank test p-value: <0.0001 (Table 1). Time-to-completion of the primary series was also faster among those who were older (≥65 years) vs. younger (<50 years, 50–64 years; $p < 0.0001$), black vs. not ($p < 0.0001$), males vs. females ($p < 0.01$), and those that had a previous chronic lung disease diagnosis vs. those that did not ($p = 0.09$). Time-to-completion of the primary series was slower among those with lower income (<$5,000/month) vs. higher income (>$5,000/month) ($p = 0.0363$) and those that were homeless vs. not ($p = 0.0075$). Among substance use behaviors, median time-to-completion of the primary series was slower among those reporting any recent injection drug use vs. none ($p < 0.0001$), non-injection stimulant use vs none ($p = 0 < 0.01$), and smoking ≥ 1 pack of cigarettes per day vs < 1 pack per day ($p = 0.09$). Results for all other variables are presented in Table 1. Kaplan-Meier product-limit survival estimates are plotted in Fig. 2 for the study sample by HIV viral load status (HIV-, HIV + [VL < 400 copies/μL], HIV + [VL ≥ 400 copies/μL]).

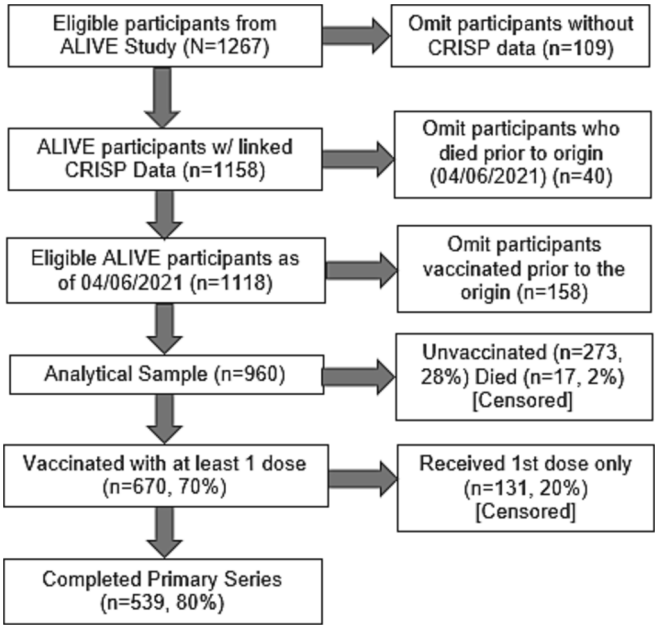

Fig. 1. Flow Diagram demonstrating ALIVE study participants that were included, omitted, censored or completed the COVID-19 vaccination primary series.

3.2. Cox Proportional Hazards modeling

In unadjusted models, the hazard of completing the COVID-19 vaccination primary series was higher among participants that were virally suppressed PWH (Hazard Ratio [HR] = 1.43, 95% 95 %CI: 1.18, 1.73) compared to participants without HIV. In the adjusted Cox Proportional Hazards model, PWH with undetectable viral load were more likely to complete the primary series (Adjusted hazards Ratio [AHR] = 1.23, 95 %CI: 1.07, 1.50) than those without HIV, after adjusting for age, race, sex, low income, homelessness, recent IDU, and recent non-IDU stimulant use (Table 2). On the other hand, PWH with higher viral loads were less likely to complete the primary series (AHR = 0.72, 95 % CI = 0.45, 1.16), when compared to participants not infected with HIV, though this association was not statistically significant. Our final model (Table 2) satisfied the proportional hazard assumption and accounted for the following variables: race, sex, age, homelessness, income, recent IDU, and recent non-IDU stimulant use.

Our sensitivity analyses supported our main findings. In a subsample restricted to PWH, we plotted time-to-vaccination and found that virally suppressed PWH demonstrated faster time-to vaccination than unsuppressed PWH (log-rank p-value: 0.016). Additionally, in a sensitivity analysis with our full analytical sample (n = 1118) with the origin set to December 12, 2020 (first day of Phase 1A eligibility), the same set of correlates of vaccination were identified and the calculated adjusted hazard ratio ratios were similar (within 5%) and remained statistically significant with the same direction of association.

4. Discussion

To our knowledge, our analysis is among the first to demonstrate an association between HIV viral load and completion of the COVID-19 vaccine primary series using objective medical record data among PWID and controlling for factors related to substance use and vaccine uptake. Overall, PWH completed the COVID-19 vaccination primary series in less time than PWID uninfected with HIV. This difference was driven by PWH who were virally suppressed. Indeed, PWH with detectable viral load were more likely to remain unvaccinated and have slower times to completion of the primary series than even participants uninfected with HIV. These findings are consistent with research in other cohorts where self-reported vaccination rates among PWH were comparable to the general population in high income countries (Fulda et al., 2022).

Our novel findings shed light on vaccine uptake behavior among PWID with HIV and highlight the critical role of care engagement for receiving HIV care and other prevention services. Previous research has identified antiretroviral adherence as a predictor for high willingness to receive the COVID-19 vaccine (Bogart et al., 2021). Sustained viral suppression, as the final stage in the HIV care continuum, implies PWH with undetectable viral load are not only linked to but also remain actively engaged in care. While in care, they may be routinely exposed to positive and accurate messaging regarding COVID-19 vaccination from a healthcare professional they trust. The opposite, then, may also be true among HIV-infected PWID with detectable HIV viral load who are disengaged or disconnected from care. Trust in one's physician has been associated with COVID-19 vaccine uptake in the general population (Viskupič et al., 2022). Social trust and confidence in health authorities with regard to specific technologies and activities like vaccination is crucial in an individual's evaluation of health-related risks and hazards. (Siegrist and Cvetkovich, 2000) PWH may also be eligible to receive supplemental services (e.g. Ryan White programs) through their HIV diagnosis which may address some structural issues related to healthcare navigation. Our findings highlight the importance of connecting PWID who are uninfected with HIV to integrated harm reduction services as there are fewer resources and opportunities to engage with healthcare outside of the context of HIV care. Additionally, interventions targeting the HIV care continuum to improve linkage to,

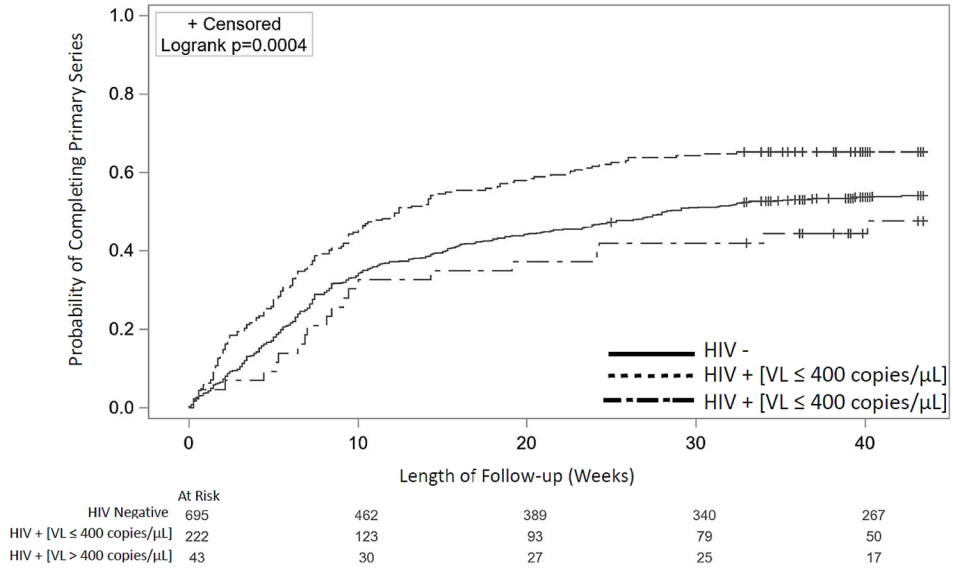

Fig. 2. Inverse Kaplan-Meier survival curve (1 – Kaplan Meier Estimate) demonstrating crude probability of completion of the COVID-19 vaccination primary series in weeks by HIV viral load status (HIV-, HIV + [VL ≤ 400 copies/μL], HIV + [VL > 400 copies/μL]).

Table 2
Unadjusted and adjusted results of Cox Proportional Hazards modeling time to completion of COVID-19 vaccination primary series among people who inject drugs in Baltimore, Maryland (n = 960).

Variable	Crude Hazard Ratio (95% CI)	Adjusted Hazard Ratio (95% CI)
HIV Infection	1.00 (ref)	1.00 (ref)
HIV -		
HIV + (VL ≤ 400 copies/μL)	1.43 (1.18, 1.73)	1.23 (1.07, 1.50)
HIV + (VL > 400 copies/μL)	0.80 (0.51, 1.26)	0.78 (0.49, 1.24)
Age Category	1.00 (ref)	1.00 (ref)
≥ 65 years		
50–64 years	0.71 (0.56, 0.92)	0.79 (0.61, 1.03)
< 50 years	0.48 (0.28, 0.51)	0.58 (0.41, 0.81)
Black (vs. not)	2.16 (1.71, 2.73)	1.66 (1.24, 2.21)
Female (vs Male)	0.75 (0.63, 0.90)	0.78 (0.64, 0.94)
Low income (≤$5k/month vs ≥)	0.82 (0.68, 0.99)	0.96 (0.79, 1.16)
Homeless (vs not)	0.70 (0.53, 0.91)	1.01 (0.72, 1.36)
Chronic Lung Disease Dx (vs no)	1.18 (0.97, 1.44)	–
Recent injection (any vs none)†	0.68 (0.56, 0.82)	0.89 (0.71, 1.11)
Recent non-injection stimulant use (vs none)†	0.77 (0.64, 0.92)	0.85 (0.70, 1.04)
Smoking ≥ 1 pack/day (vs < 1 pack/day)†	0.82 (0.65, 1.03)	–

†Previous six months.

receipt of, and retention in care in this population are warranted and may synergize with efforts to improve vaccination among PWID living with HIV.

Our analysis controlled for older age (Burke et al., 2021) and higher income (McKinnon et al., 2021) as significant correlates of vaccine uptake, consistent with trends elsewhere. Our final model also accounted for homelessness and substance use, consistent with previous research that has highlighted the structural barriers to both viral suppression and vaccination among people experiencing poverty, homelessness, and active injecting (Cioffi et al., 2022; Arcadepani et al., 2021; Montgomery et al., 2022; Lockett et al., 2021) In addition to individual hesitancy, barriers to vaccination for PWID may include competing priorities and availability issues such as staffing at community-based and harm reduction sites. (Montgomery et al., 2022) In concert with HIV maintenance for HIV-infected PWID, interventions targeting substance use behaviors and social determinants (i.e. poverty, homelessness) may be warranted to improve vaccine uptake among vulnerable PWID. These may include vaccination sites embedded in PWID communities (e.g. syringe service programs), linkage with health teams, and the accompaniment of key resources (e.g. housing, food, incentives, technology support, social services). (Arcadepani et al., 2021; Dai et al., 2021).

Our analysis has several notable strengths including laboratory-confirmed data on viral load status as well as date of receipt of vaccination and manufacturer type from what is considered the gold standard source for vaccination status in Maryland. (Cepeda et al., 2022) However, there are several limitations. Our conservative approach in selecting April 6, 2021 (Phase 3 general eligibility) as the origin for the survival analysis instead of December 12, 2020 (first day of Phase 1A select eligibility) may have excluded many who had early eligibility and were vaccinated prior to the origin. For this reason, many of our findings might be considered underestimates of the true effects. Results from our sensitivity analysis using December 12, 2020 as the origin, however, support the main effects demonstrated in our adjusted analysis. We did not have detailed enough data on employment to infer vaccine eligibility data, but we examined employment status to account for potential effects of work-related eligibility and mandates. Interestingly, this was not statistically significant in both our main findings and the sensitivity analysis, suggesting that work-related vaccine eligibility may not have been a significant factor in determining vaccine uptake in our sample of PWID. As several of our variables of interest were time-fixed, our analysis was unable to account for changes that may have occurred during the follow-up period in our analysis. This was due to changes in data collection as study clinic operations were altered in response to the COVID-19 pandemic.

Our findings should be interpreted in light of shifting dynamics in substance use and other relevant factors due to the COVID-19 pandemic. Future research should also account for COVID-19 booster shots which have become increasingly relevant since the emergence of the highly transmissible Omicron variant. However, there is no evidence in our analysis to suggest that future booster doses would be different in our cohort compared to the general population considering that overall vaccination and the proportion of those completing the primary series was comparable to the general population in Maryland at the time of data abstraction. Given that the uptake of COVID-19 booster doses has been relatively low in the general population, future efforts to examine time-to-vaccination for additional COVID-19 doses, including variant-specific boosters, among PWH and PWID is warranted.

This analysis highlights the significant role of HIV viral suppression among PWID as a correlate of increasing COVID-19 vaccine uptake compared to those with unsuppressed HIV viral load. This understanding is especially relevant given the competing barriers to care experienced by this population including socio-structural factors (i.e. poverty, homelessness) and substance use behaviors (active injecting, stimulant use). While additional research is warranted in the context of HIV, injection drug use and COVID-19 prevention; our findings support interventions targeting both socio-structural barriers to care as well as interventions to improve the HIV care continuum for the added value of healthcare engagement and COVID-19 vaccine uptake.

Author Contributions

All authors made major contributions to the project including conceptualization, conduct of the analysis, and manuscript development. PB led all aspects of the analysis and scientific writing/editing. JC and BG contributed to analysis supervision, analysis interpretation, and writing/editing. CS and JA contributed to project administration, data curation and validation. KF, JR, and JS contributed to conceptualization, analysis interpretation and manuscript writing/editing. SM and GK contributed analysis supervision, funding acquisition, and manuscript editing.

Disclosure of Funding

Grant support was provided by the National Institute on Drug Abuse (U01-DA-036297 [GDK, SHM], T32-AI-102623 [PB] and R01-DA-053136 [BG]) and National Institute of Allergy and Infectious Diseases (NIAID, K01-AI-162247 [JS]). This analysis resulted (in part) from research supported by the Johns Hopkins University Center for AIDS Research, an NIH funded program (1P30AI094189), which is supported by the following NIH Co-Funding and Participating Institutes and Centers: NIAID, NCI, NICHD, NHLBI, NIDA, NIA, NIGMS, NIDDK, NIMHD. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

CRediT authorship contribution statement

Pieter Baker: Conceptualization, Software, Formal analysis, Investigation, Writing – original draft, Visualization. **Javier A Cepeda:** Conceptualization, Investigation, Writing – review & editing, Supervision. **Catherine Schluth:** Resources, Project administration. **Jacquie Astemborski:** Software, Data curation, Project administration. **Kenneth A. Feder:** Conceptualization, Writing – review & editing, Project administration. **Jacqueline Rudolph:** Writing – review & editing. **Jing Sun:** Writing – review & editing. **Gregory D. Kirk:** Supervision, Project administration, Funding acquisition, Writing – review & editing. **Shruti H. Mehta:** Supervision, Project administration, Funding acquisition, Writing – review & editing. **Becky L. Genberg:** Conceptualization, Investigation, Writing – review & editing, Supervision.

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.

Data availability

The authors do not have permission to share data.

References

Andreas, M., Iannizzi, C., Bohndorf, E., Monsef, I., Piechotta, V., Meerpohl, J.J., Skoetz, N., 2022. Interventions to increase COVID-19 vaccine uptake: a scoping review. Cochrane Database of Systematic Reviews 2022 (8).

Ao, G., Li, T., Wang, Y., Li, J., Tran, C., Chen, M., Qi, X., 2022. Opioid usage and COVID-19 prognosis: A systematic review and meta-analysis. The American Journal of Emergency Medicine 56, 51–56.

Arcadepani, F.B., De Macedo, M.A.C.F., Tardelli, V.S., Martins, S.S., Fidalgo, T.M., 2021. COVID-19 vaccination among socially vulnerable people who use drugs. Addiction 116 (9), 2590–2591.

Bogart, L.M., Ojikutu, B.O., Tyagi, K., Klein, D.J., Mutchler, M.G., Dong, L.u., Lawrence, S.J., Thomas, D.R., Kellman, S., 2021. COVID-19 related medical mistrust, health impacts, and potential vaccine hesitancy among black americans living with HIV. Journal of Acquired Immune Deficiency Syndromes 86 (2), 200–207.

Burke, P.F., Masters, D., Massey, G., 2021. Enablers and barriers to COVID-19 vaccine uptake: An international study of perceptions and intentions. Vaccine 39 (36), 5116–5128.

Cepeda, J.A., Feder, K.A., Astemborski, J., Schluth, C., Kirk, G.D., Mehta, S.H., Genberg, B.L., 2022. COVID-19 vaccine hesitancy and vaccination status in a Community-Based cohort of people who inject drugs in baltimore, maryland, march–June 2021. Public Health Reports. 137 (5), 1031–1040.

Childs K, Post FA, Norcross C, et al. Hospitalized Patients With COVID-19 and Human Immunodeficiency Virus: A Case Series. *Clin Infect Dis.* 2020;71(8):2021-2022.

Cioffi, C.C., Kosty, D., Nachbar, S., Capron, C.G., Mauricio, A.M., Tavalire, H.F., 2022. COVID-19 vaccine deliberation among people who inject drugs. Drug Alcohol Depend Rep. 3, 100046.

Csete, J., Kamarulzaman, A., Kazatchkine, M., Altice, F., Balicki, M., Buxton, J., Cepeda, J., Comfort, M., Goosby, E., Goulão, J., Hart, C., Kerr, T., Lajous, A.M., Lewis, S., Martin, N., Mejía, D., Camacho, A., Mathieson, D., Obot, I., Ogunrombi, A., Sherman, S., Stone, J., Vallath, N., Vickerman, P., Zábranský, T., Beyrer, C., 2016. Public health and international drug policy. The Lancet. 387 (10026), 1427–1480.

Dai, H., Saccardo, S., Han, M.A., Roh, L., Raja, N., Vangala, S., Modi, H., Pandya, S., Sloyan, M., Croymans, D.M., 2021. Behavioural nudges increase COVID-19 vaccinations. Nature 597 (7876), 404–409.

Degenhardt, L., Peacock, A., Colledge, S., Leung, J., Grebely, J., Vickerman, P., Stone, J., Cunningham, E.B., Trickey, A., Dumchev, K., Lynskey, M., Griffiths, P., Mattick, R.P., Hickman, M., Larney, S., 2017. Global prevalence of injecting drug use and sociodemographic characteristics and prevalence of HIV, HBV, and HCV in people who inject drugs: a multistage systematic review. The Lancet Global Health. 5 (12), e1192–e1207.

Dong, E., Du, H., Gardner, L., 2020. An interactive web-based dashboard to track COVID-19 in real time. The Lancet Infectious Diseases 20 (5), 533–534.

Dunlop, A., Lokuge, B., Masters, D., Sequeira, M., Saul, P., Dunlop, G., Ryan, J., Hall, M., Ezard, N., Haber, P., Lintzeris, N., Maher, L., 2020. Challenges in maintaining treatment services for people who use drugs during the COVID-19 pandemic. Harm Reduction Journal. 17 (1).

Fulda ES, Fitch KV, Overton ET, et al. COVID-19 Vaccination Rates in a Global HIV Cohort. *The Journal of Infectious Diseases.* 2022;225(4):603-607.

Hiv, T.L., 2021. Prioritise people with HIV for COVID-19 vaccination. The Lancet HIV. 8 (11), e659.

Jaiswal, J., Krause, K.D., Martino, R.J., D'Avanzo, P.A., Griffin, M., Stults, C.B., Karr, A. G., Halkitis, P.N., 2022. SARS-CoV-2 vaccination hesitancy and behaviors in a national sample of people living with HIV. AIDS Patient Care and STDs 36 (1), 34–44.

Lockett, H., Koning, A., Lacey, C., et al., 2021. Addressing structural discrimination: prioritising people with mental health and addiction issues during the COVID-19 pandemic. The New Zealand Medical Journal 134 (1538), 128–134.

Mathieu, E., Ritchie, H., Ortiz-Ospina, E., Roser, M., Hasell, J., Appel, C., Giattino, C., Rodés-Guirao, L., 2021. A global database of COVID-19 vaccinations. Nature Human Behaviour. 5 (7), 947–953.

McCree, D.H., Beer, L., Jeffries, W.L., Tie, Y., Fagan, J., Crim, S.M., 2021. Sociodemographic correlates of self-reported discrimination in HIV health care settings among persons with diagnosed HIV in the united states, medical monitoring project, 2018–2019. Journal of Acquired Immune Deficiency Syndromes 88 (5), 457–464.

McKinnon, B., Quach, C., Dubé, È., Tuong Nguyen, C., Zinszer, K., 2021. Social inequalities in COVID-19 vaccine acceptance and uptake for children and adolescents in montreal. Canada. *Vaccine.* 39 (49), 7140–7145.

Mohammed, A.H., Blebil, A., Dujaili, J., Rasool-Hassan, B.A., 2020. The risk and impact of COVID-19 pandemic on immunosuppressed patients: Cancer, HIV, and solid organ transplant recipients. AIDS Reviews 22 (3), 151–157.

Montgomery, M.P., Zhong, Y., Roberts, E., Asher, A., Bixler, D., Doshani, M., Christensen, A., Eckert, M., Weng, M.K., Carry, M., Samuel, C.R., Teshale, E.H., 2022. Vaccination barriers and opportunities at syringe services programs in the united states, June-August 2021-A cross-sectional survey. Drug and Alcohol Dependence 237, 109540.

Nomah, D.K., Reyes-Urueña, J., Díaz, Y., et al., 2021. Sociodemographic, clinical, and immunological factors associated with SARS-CoV-2 diagnosis and severe COVID-19 outcomes in people living with HIV: a retrospective cohort study. Lancet HIV. 8 (11), e701–e710.

Plummer, M.M., Pavia, C.S., 2021. COVID-19 vaccines for HIV-Infected patients. Viruses 13 (10), 1890.

Prevention CfDCa. COVID Data Tracker. US Department of Health and Human Services. https://covid.cdc.gov/covid-data-tracker. Published 2022. Accessed September 26.

Qi, L., Yang, L., Ge, J., Yu, L., Li, X., 2021. COVID-19 vaccination behavior of people living with HIV: the mediating role of perceived risk and vaccination intention. Vaccines. 9 (11), 1288.

Quinn, B., Gorbach, P.M., Okafor, C.N., Heinzerling, K.G., Shoptaw, S., 2020. investigating possible syndemic relationships between structural and drug use

factors, sexual HIV transmission and viral load among men of colour who have sex with men in los angeles county. Drug and Alcohol Review. 39 (2), 116–127.

Rane MS, Kochhar S, Poehlein E, et al. Determinants and Trends of COVID-19 Vaccine Hesitancy and Vaccine Uptake in a National Cohort of US Adults: A Longitudinal Study. *American Journal of Epidemiology.* 2022;191(4):570-583.

Robinson, E., Jones, A., Lesser, I., Daly, M., 2021. International estimates of intended uptake and refusal of COVID-19 vaccines: A rapid systematic review and meta-analysis of large nationally representative samples. Vaccine 39 (15), 2024–2034.

Siegrist, M., Cvetkovich, G., 2000. Perception of hazards: the role of social trust and knowledge. Risk Analysis. 20 (5), 713–720.

Ssentongo, P., Heilbrunn, E.S., Ssentongo, A.E., Advani, S., Chinchilli, V.M., Nunez, J.J., Du, P., 2021. Epidemiology and outcomes of COVID-19 in HIV-infected individuals: a systematic review and meta-analysis. Scientific Reports. 11 (1).

Sun, J., Mehta, S.H., Astemborski, J., Piggott, D.A., Genberg, B.L., Woodson-Adu, T., Benson, E.-M., Thomas, D.L., Celentano, D.D., Vlahov, D., Kirk, G.D., 2022. Mortality among people who inject drugs: a prospective cohort followed over three decades in baltimore, MD. USA. *Addiction.* 117 (3), 646–655.

Valasek, C.J., Streuli, S.A., Pines, H.A., Mittal, M.L., Strathdee, S.A., Vera, C.F., Harvey-Vera, A., Bazzi, A.R., 2022. COVID-19 vaccination acceptability and experiences among people who inject drugs in san diego county. Preventive Medical Reports 30, 101989.

Viskupič, F., Wiltse, D.L., Meyer, B.A., 2022. trust in physicians and trust in government predict COVID-19 vaccine uptake. Social Science Quarterly. 103 (3), 509–520.

Viswanath, K., Bekalu, M., Dhawan, D., Pinnamaneni, R., Lang, J., Mcloud, R., 2021. Individual and social determinants of COVID-19 vaccine uptake. BMC Public Health 21 (1).

Vlahov, D., Anthony, J.C., Munoz, A., et al., 1991. The ALIVE study, a longitudinal study of HIV-1 infection in intravenous drug users: description of methods and characteristics of participants. NIDA Research Monograph 109, 75–100.

Wickersham, J.A., Meyer, J.P., Shenoi, S., Altice, F.L., Barakat, L.A., Virata, M., Olivares, M., Maviglia, F., Khati, A., Shrestha, R., 2022. Willingness to be vaccinated against COVID-19 among people with HIV in the united states: Results from a national survey. Front Med (Lausanne). 9, 886936.

Yang, X., Sun, J., Patel, R.C., Zhang, J., Guo, S., Zheng, Q., Olex, A.L., Olatosi, B., Weissman, S.B., Islam, J.Y., Chute, C.G., Haendel, M., Kirk, G.D., Li, X., Moffitt, R., Akelsrod, H., Crandall, K.A., Francheschini, N., French, E., Po-Yu Chiang, T., Caleb-Alexander, G., Andersen, K.M., Vinson, A.J., Brown, T.T., Mannon, R.B., 2021. Associations between HIV infection and clinical spectrum of COVID-19: a population level analysis based on US national COVID cohort collaborative (N3C) data. Lancet HIV. 8 (11), e690–e700.