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Impact of Pandemic-Induced Service Disruptions and Behavioral Changes on Hepatitis C Virus and HIV Transmission Amongst People Who Inject Drugs: A Modeling Study

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Background. The coronavirus disease 2019 (COVID-19) pandemic may have disproportionally impacted vulnerable groups such as people who inject drugs (PWID) through reduced health care services as well as social changes from pandemic mitigation measures. Understanding how the COVID-19 pandemic and associated mitigation strategies subsequently changed the trajectory of hepatitis C virus (HCV) and human immunodeficiency virus (HIV) transmission is critical to estimating disease burdens, identifying outbreak risk, and developing informed intervention strategies.

Methods. Using behavioral data from the AIDS Linked to the IntraVenous Experience (ALIVE) study, an ongoing community-based cohort of PWID in Baltimore, United States, and an individual-based network model, we explored the impacts of service disruptions combined with changes in social networks and injecting behaviors of PWID on HCV and HIV transmission.

Results. Analyses of ALIVE data showed that during the pandemic, there was an acceleration in injection cessation trajectories but those who continued injecting increased the frequency of injection; at the same time, individual drug-use networks became smaller and the probability of injecting with others decreased. Simulation results demonstrated that HCV and HIV prevalence increased from service disruptions alone, but these effects were mitigated when including observed behavior changes in addition.

Conclusions. Model results combined with rich individual behavioral data indicated that pandemic-induced behavioral changes of PWID that lasted longer than service disruptions could have offset the increasing disease burden caused by disrupted services during the pandemic.

Keywords: mathematical model; COVID-19; people who inject drugs; hepatitis C; HIV.

During the early stages of the coronavirus disease 2019 (COVID-19) pandemic, there were global disruptions to health care services [1, 2], from the implementation of nonpharmaceutical interventions such as stay-at-home orders and social distancing measures [3, 4]. These factors led to general concerns about increases in hepatitis C virus (HCV) and human immunodeficiency virus (HIV) transmission amongst high-risk populations such as people who inject drugs (PWID). Across the United States, access to clinical services such as HCV/HIV testing and treatment, as well as harm-reduction services, including syringe service programs (SSP) and medication for opioid use disorder (MOUD), were temporarily closed, scaled down with limited operating hours and capacities, or shifted to new policies surrounding service delivery of which PWID had limited awareness [5–7]. Consequently, risk factors such as low stock of opioid-agonist treatment and clean syringes were reported by PWID during this time [8–10], along with lower rates of HCV and HIV testing [11, 12], HCV treatment initiation [13], receipt of prevention such as pre-exposure prophylaxis [12], and HCV or HIV care retention [14, 15] across geographic settings and demographic groups [16]. In addition, changes to drug markets with supply chain disruptions may have also impacted drug-use behavior [17].

These factors could impact HCV and HIV transmission amongst PWID. For example, an increase in HIV prevalence among PWID over 2019–2021 was reported in Greece with heightened risk associated with individuals sharing syringes [18], and a phylogenetic analysis in Canada showed rapid growth of HIV transmission clusters associated with PWID [17]. Mathematical modeling results consistently supported these ideas with multiple studies estimating an increased disease burden following pandemic-induced service disruptions

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[13, 19–22]. Despite these predictions, few locations in the United States have reported substantial increases in HCV/HIV prevalence since the COVID-19 pandemic, creating discrepancies between observed data and modeling results. This discrepancy may be explained in part by the underascertainment of HCV and HIV diagnoses during the pandemic: while HIV surveillance data from the Centers for Disease Control and Prevention (CDC) showed an 18% increase in HIV diagnoses in the United States from 2020 to 2021, it was likely due to HIV diagnoses missed in 2020 [23]. It is also likely that models examining impacts of the pandemic on HCV and HIV underestimated the impact of behavioral changes that occurred during this time. In a multilevel framework, changes to the mezzoenvironment (service delivery landscape), as well as the microenvironment (individual behaviors and drug injection networks), could both impact the health outcomes of PWID [24].

Consistently, models assumed that risky behaviors of PWID remained static during the pandemic, with only a few modeling projections exploring how hypothetical changes in social and injecting behaviors could impact HIV incidence amongst PWID in addition to service closures [19, 25]. However, to date, there have been few analyses focused on the complex behavioral dynamics driving transmission amongst PWID during the COVID-19 pandemic. Some evidence showed a decrease in injection drug use along with increases in injection frequency and the likelihood of using drugs alone [8, 9, 26], which could be the compound effect of voluntary social distancing, social/economic instability, and disruptions to the drug market. However, less was known about to what extent this could impact disease transmission. Understanding how changes in drug-use networks and individual injecting behaviors may influence HCV and HIV transmission dynamics can help understand observed trends. Our study aimed to incorporate factors in both mezzoenvironment and microenvironment impacts to estimate changes to the HCV/HIV burden amongst PWID.

Here, we developed an empirically grounded model of HCV and HIV transmission among a population of PWID like the AIDS Linked to the Intravenous Experience (ALIVE) study cohort in Baltimore. We constructed a stochastic individual-based network of simulated HCV and HIV transmission considering pandemic-induced service disruptions. Using drug-use network data and behavioral surveys of ALIVE participants pre- and post-pandemic, we tested the hypothesis that changes in drug-use networks and injecting behavior can mitigate or even offset the impact of service disruptions on HCV and HIV transmission compared with models that did not incorporate these changes.

METHODS

ALIVE Study Data Overview

Our study used empirical data from a subset of participants enrolled in the ALIVE study [27]. ALIVE is an ongoing community-based cohort in Baltimore, Maryland, United States that beginning in 1988–1989, has had 5 additional recruitment waves (1994–1995, 1998, 2000, 2005–2008, and 2015–2018). To date, the cohort has recruited over 5700 adults ≥18 years of age who reported a history of injection drug use. Participants are followed every 6 months with routine questionnaires to assess sociodemographic characteristics, substance use behaviors, and health status, and to collect biospecimens. Here, we focused on participants with routine ALIVE visits between January 2014 and August 2023 and were alive by March 2020 (n = 1439). Variables used included sociodemographic characteristics, recent injection drug use behaviors including injection frequency in the prior 6 months, access to harm-reduction services (eg, methadone, buprenorphine, and SSP), and ART use, as well as HCV and HIV viral loads from biospecimens. We also included data from social network surveys from 2 periods (November 2018–November 2019, n = 238 and June 2022–August 2023, n = 592) assessing participants' drug-use networks as well as characteristics of their drug-use partners. In this egocentric network survey, respondents represented egos and nominated drug-use partners were alters. Questions used to included the ages of ego and alters, number of drug-use partnerships, frequency of injecting with drug-use partners, frequency of syringe sharing, and duration of partnerships [28].

The Johns Hopkins University Institutional Review Board has continuously approved the ALIVE study. All study procedures were conducted in accordance with Johns Hopkins University Institutional Review Board's standards and the Declaration of Helsinki. All participants provided written informed consent.

Individual-Based Network Model Structure

We adapted and extended the R package *EpiModel* modeling framework [29] to build a dynamic network-based model of HCV and HIV transmission within a hypothetical population of approximately 10 000 PWID with similar characteristics to the ALIVE cohort (Figure 1 and Supplementary Material). The code for the model can be found at https://github.com/ywang692/PWID_ALIVE_model. Parameters were informed by cross-sectional analyses of the ALIVE survey data, when possible, as well as estimates from existing literature (details about data source, uncertainty, and calibration of parameter values can be found in Supplementary Tables 1 and 2). A temporal extended random graph model was used to simulate the dynamic and heterogeneous nature of injecting partnerships, where nodes were individuals and edges represented injecting partnerships (see "Methods" in Supplementary Material). Baseline characteristics of individuals were assigned either with fixed values or from probability distributions to account for heterogeneity within the population (Supplementary Table 1). At each time point, the probability an individual was actively injecting was based on 4 injection risk trajectories previously identified [30]. Individuals could enter the population through the initiation

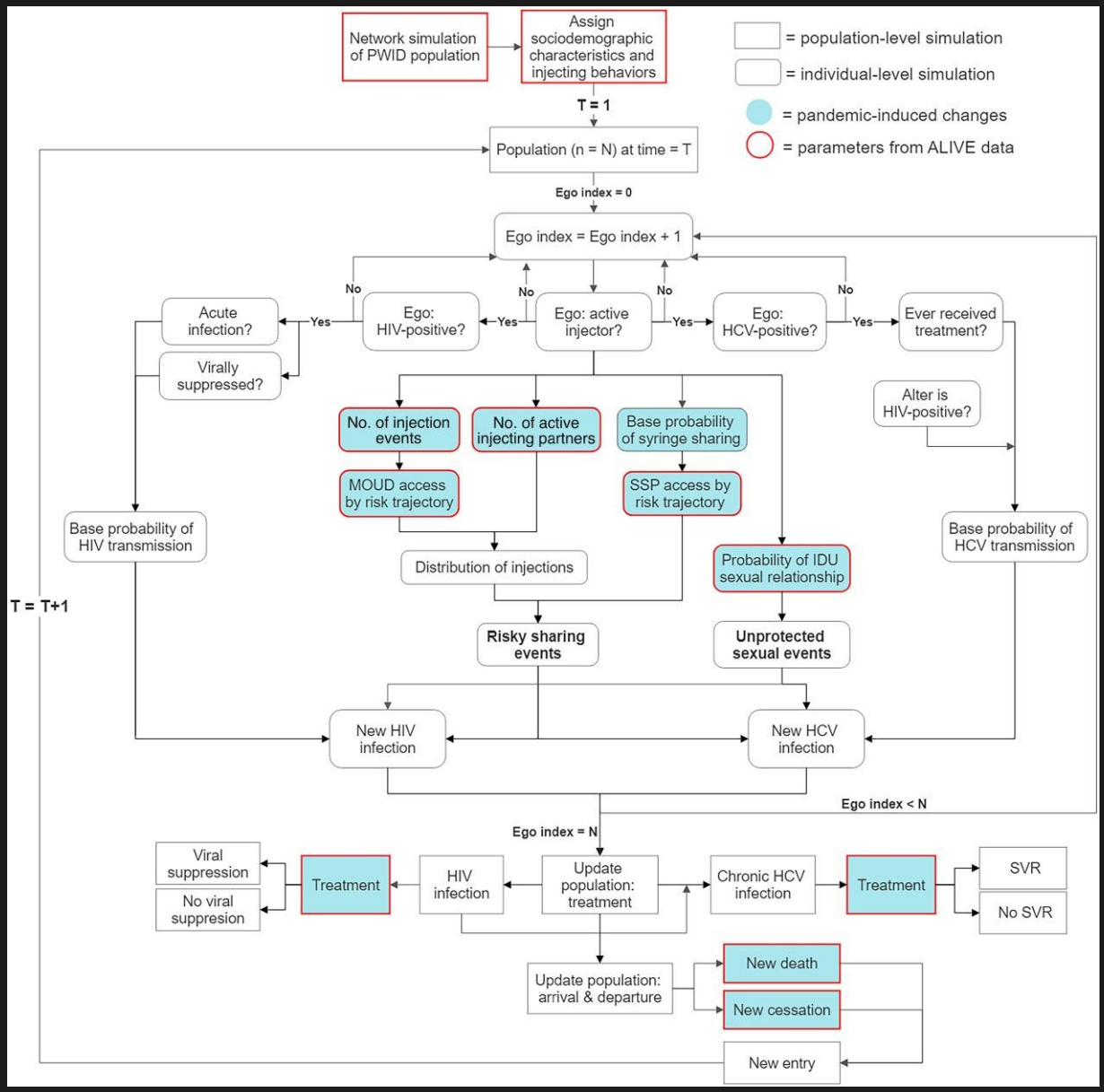

Figure 1. Schematic description of an individual-based network model simulation of HCV and HIV transmission amongst PWID. We modeled HCV and HIV transmission amongst PWID in a population like the ALIVE cohort (Supplementary Material). Each actively injecting ego was assigned a risk trajectory and injection frequency. If infected by HCV and/or HIV, an ego's injecting events or sexual acts with alters could result in disease transmission. Given the number of risky shared injections or sexual acts, infection events were modeled by a binomial distribution with (1) the number of trials dictated by the frequency of shared injections/sexual acts between the ego-alter pair and their access to harm-reduction service; and (2) the probability of infection being the product of baseline per-act transmission rate and multipliers including acute infection and coinfection. After simulations of potential transmission between each infected-susceptible pair, testing and treatment were simulated, followed by arrivals (initiation of injection drug use), departures (death), and cessation/relapse based on individuals' injection risk trajectory. N was the size of active injector population (n) at a current simulation cycle, and T was the time step of the current simulation cycle. Abbreviations: ALIVE, AIDS Linked to the IntraVenous Experience; HCV, hepatitis C virus; HIV, human immunodeficiency virus; IDU, injection drug use; MOUD, medication for opioid use disorder; PWID, people who inject drugs; SSP, syringe service programs; SVR, sustained virologic response. Figure created using SmartDraw Software.

of injection drug use or leave the population with age-specific, disease-status-specific mortality rates derived from ALIVE (Supplementary Material). Simulations were run for 10 years starting in March 2018, accounting for 2 years of pre–COVID-19 pandemic period (2018–2020), early (2020–2021), and late periods (2021–2023), with 5 additional years to explore longer-lasting pandemic-induced changes. Two hundred-simulations were run for each scenario.

Simulating Disease Transmission and Services

Two routes of HCV and HIV infection were considered: parenteral exposure by sharing injecting paraphernalia and mucosal

exposure via sexual transmission. We primarily focused on transmission through injecting partnerships and only considered sexual transmission within overlapping injecting partnerships (details in Supplementary Material); the probability of having multiple (ie, injecting and sexual) ties differed by gender (Supplementary Table 3). The initial chronic HCV infection prevalence (defined by detectable HCV RNA) within active PWID was 46.7% in 2018 (Supplementary Figure 1A). Upon incident infection, one could spontaneously clear HCV during the acute infection phase or reach sustained virologic response once treated. The initial HIV prevalence within actively injecting PWID was 22.9% in 2018 (Supplementary Figure 1B). The risk of HCV and HIV transmission was higher when a newly infected individual was in their acute phase. Initiation of ART decreased the base transmission probability by different rates with or without successful viral suppression. In the event of HCV/HIV coinfection, an individual with HIV infection was more likely to acquire HCV infection and less likely to spontaneously clear an acute HCV infection; successful HIV viral suppression was also harder to achieve for coinfected individuals [31]. The model was calibrated to the reported HCV and HIV active infection prevalence in the ALIVE cohort from 2018 to 2019 (Supplementary Figure 1 and Supplementary Table 2). Adoption of harm-reduction services was correlated with an individual's risk trajectory based on ALIVE survey results (Supplementary Material).

RESULTS

Service Disruptions Increased Both HCV and HIV Burden Amongst PWID

We considered a combination of disruptions in health care services reported during the COVID-19 pandemic over multiple durations (3–12 months) and impact (0%–100% disrupted) based on nationwide reports and additional studies (Table 1). We assumed that service disruptions initiated in March 2020 in all simulations and returned to normal coverages after respective disruption durations.

We simulated HCV and HIV transmission with disruptions occurring when the majority of nonpharmaceutical interventions were implemented in the United States (March 2020) until our most recent ALIVE postpandemic survey (August 2023). Assuming there was no impact from the COVID-19 pandemic (baseline scenario; Figure 2), HCV prevalence was estimated to be 42.6% (95% confidence interval [CI] from repeated simulations, 42.4%–42.7%) with an incidence of 8.97 (95% CI, 8.83–9.12) cases per 100 person-years (PY), and HIV prevalence 23.4% (95% CI, 23.2%–23.5%) with 2.21 (95% CI, 2.15–2.26) incident cases per 100 PY. Until August 2023, pandemic-induced service disruptions (Table 1) increased the prevalence of both HCV and HIV ($P < .01$; Figure 2) to a mean HCV prevalence of 44.1% (95% CI, 43.9%–44.3%) and mean HIV prevalence of 24.3% (95% CI, 24.1%–24.4%), 1.5% and 0.9% above baseline, respectively. HCV and HIV incidence increased to 11.50 (95% CI, 11.38–11.63) and 3.16 (95% CI, 3.10–3.22) per 100 PY in 2020 ($P < .01$), then dropped back to around baseline levels in 2021.

In addition to the combined impact of all reported service disruptions, we conducted sensitivity analyses comparing the impact of each individual service disruption by setting the duration of 1 service disruption to 100% for 12 or 24 months and keeping the rest at their prepandemic coverage. Temporary disruption of each service individually could lead to an increase in HCV and HIV prevalence by the end of 2023 with the overall impact positively related to the duration of disruption (Supplementary Figure 2). Disruption of HCV testing and treatment led to the largest increase in HCV prevalence (12-month average of 5.4% increase over baseline; 95% CI, 5.1%–5.6%; Supplementary Figure 4), followed by MOUD (12-month average of 2.8% increase over baseline; 95% CI, 2.7%–3.0%). The slope of prevalence increase did not differ significantly between the first and second years of service disruption. Similarly, disruption of HIV testing and treatment led to the biggest increase in HIV prevalence (Supplementary Figure 3), with a 12-month increase of 4.5% (95% CI, 4.3%–4.8%; $P < .05$). MOUD disruptions had the second largest impact on HIV prevalence, resulting in a 12-month increase of 1.5% (95% CI, 1.3%–1.7%).

Table 1. Lengths and Magnitudes of COVID-19 Pandemic-Induced Service Disruptions Considered in Each Simulation

Service Disruptions	Values	Source
SSP	Complete closure 3 mo + 50% partial capacity 9 mo	[32]
MOUD	Complete closure 3 mo + 50% partial capacity 9 mo	Assumed to be same as SSP
HIV testing	32%–86% partial capacity 3 mo	[12, 33, 34]
ART prescription	Minimal disruption	[12]
HCV treatment (DAA)	50% partial capacity 3 mo+ 70% partial capacity 9 mo	[35]

Abbreviations: ART, antiretroviral therapy; DAA, direct-acting antiviral; HCV, hepatitis C virus; MOUD, medication for opioid use disorder; SSP, syringe service program.

Since the COVID-19 Pandemic, PWID Reduced the Probability of Injection Drug Use and the Number of Injecting Partnerships

Leveraging data from the ALIVE study, we further explored how individual behaviors may have changed during the COVID-19 pandemic using pre- and postpandemic routine survey data from 1439 individuals (predates, 6 January 2014 to 28 February 2020; postdates, 7 December 2020 to 31 August 2023). Compared to the prepandemic survey, significantly fewer participants reported injecting at least once in the past 6 months of their latest visit, from 34.3% (485/1416) to 15.1% (126/833, $P < .01$). However, of those who reported injecting within the past month, the frequency of injection increased by 44%, from 23.5 (95% CI, 21.3–25.6) per month

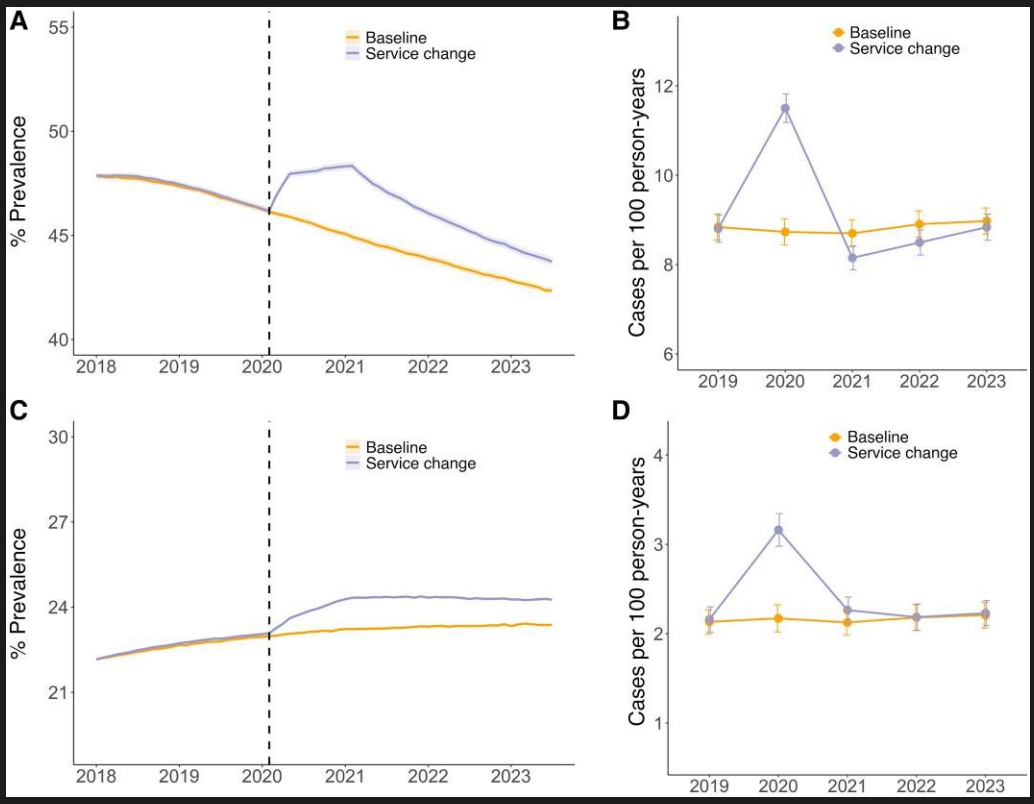

Figure 2. The estimated prevalence and incidence of HCV and HIV from simulations. Prevalence and incidence of HCV (*A* and *B*) and HIV (*C* and *D*) from the beginning of the COVID-19 pandemic (March 2020, dashed line) to the most recent ALIVE social network survey period (August 2023) were compared across 2 scenarios: (1) baseline scenario ("baseline," yellow) where no pandemic or subsequent responses took place; and (2) service disruption-only scenario ("service change," purple) where the COVID-19 pandemic took place and clinical/harm-reduction services were disrupted in their respective durations and magnitudes as reported in Table 1. The lines and solid dots represent mean values of 200 repeated simulations; the shaded areas around the lines and error bars on solid dots represent 95% confidence intervals. Abbreviations: ALIVE, AIDS Linked to the IntraVenous Experience; COVID-19, coronavirus disease 2019; HCV, hepatitis C virus; HIV, human immunodeficiency virus.

prepandemic to 33.8 (95% CI, 28.7–38.9) times per month postpandemic ($P < .01$; Figure 3B). Previously, we classified individuals into injection risk categories based on individuals' probability of drug injection throughout their drug-use history (early cessation, delayed cessation, persistent injection, and frequent relapse) [30]. Briefly, for individuals in the early cessation trajectory, the probability of injection drug use decreases quickly since their first injection. This decrease is slower for those in delayed cessation and nonexistent for those in persistent injection trajectory; those in frequent relapse trajectory tend to oscillate between active drug use and temporary cessation and thus are assumed to always have a 50% probability of injection drug use. Using data from 325 individuals who had at least 2 prepandemic study visits and 2 postpandemic study visits and had reported active injection drug use in at least 1 of those visits, we identified their injection risk trajectories and found that there was a higher proportion of participants classified in the early cessation trajectory postpandemic (postpandemic 57.5% compared to prepandemic 43.1%); the other trajectories all decreased in their frequency amongst the participants (Figure 3A). These shifts primarily occurred within "delayed cessation" (90.2%) or "frequent relapse" (54.0%) individuals switching to "early cessation" postpandemic (Supplementary Table 4).

Finally, we analyzed egocentric data from a subset of ALIVE social network survey participants to explore how their drug-use networks and injecting behaviors with partners changed during the pandemic ($n_{pre} = 238$, November 2018 to August 2019 vs $n_{post} = 592$, June 2022 to August 2023). Overall, for those reporting injection drug use in the prior 6 months in their prepandemic versus postpandemic social network survey ($n_{pre} = 179$, $n_{post} = 92$), the median number of drug-use alters per participant decreased from 3 (prepandemic) to 1 (postpandemic) ($P < .01$; Figure 3C) and the probability of ever injecting with their drug-use alters decreased from 81.5% prepandemic to 59.2% postpandemic ($P < .01$; Figure 3D). In addition, the probability of syringe sharing with injecting partners also decreased from 22.0% to 11.4%, although the change was not statistically significant ($P = .08$; Supplementary Figure 5). Similar trends were observed when comparing individuals in both pre- and postpandemic surveys (n = 104) (Supplementary Figure 6). Participants of the postpandemic

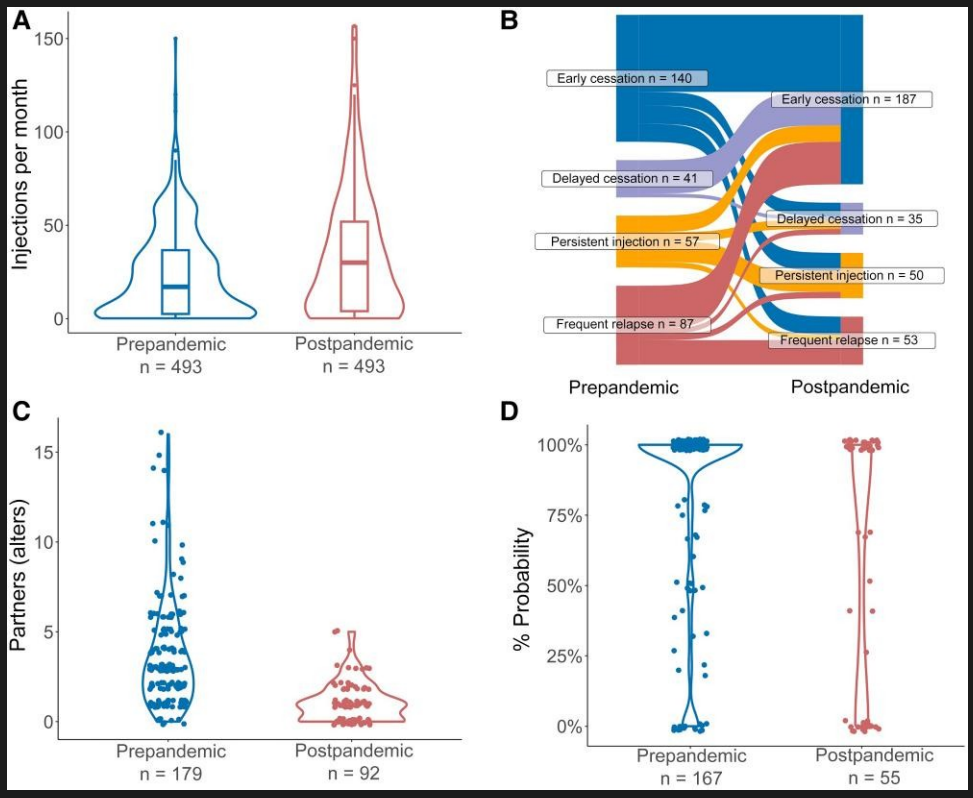

Figure 3. Reported changes in social and injecting behaviors amongst AIDS Linked to the IntraVenous Experience (ALIVE) participants prepandemic versus postpandemic. *A*, Comparison of survey participants' monthly injecting frequency. Line, box, and whiskers represent median, interquartile range, and lower/upper fences excluding outliers, respectively; the outer shapes represent distribution of individual data points. *B*, Changes in survey participants' probability of active injection reflected by the changing distribution of 4 injection risk trajectories. *C*, Comparison of the numbers of drug-use partners (alters) in the prior 12 months. *D*, Comparison of probability distributions of survey participants reporting injecting with drug-use partners. For *C* and *D*, each solid dot represents an individual data point, and the lined shapes represents distribution of all data points.

social network survey were also asked whether they still used drugs with alters they named during their prepandemic social network surveys. Among participants who were surveyed in both pre- and postpandemic periods, a total of 99 prepandemic edges were reported with 18 of the edges still active after a mean of 52 months between the 2 surveys. The rate of edge dissolution was calculated to be 1.57% of total edges per month, with the mean edge duration being 63.6 months.

PWID Behavioral Changes Observed During the COVID-19 Pandemic Offset Increases in Disease Burden Due to Service Disruptions

We then simulated HCV and HIV transmission with both service disruptions and PWID behavioral changes identified above. We assumed that behavioral changes occurred from March 2020 until the last enrollment of the postpandemic social-network survey (August 2023). Approximately 40% of the prepandemic participants were lost to follow-up postpandemic and thus their behavioral changes could not be measured. To estimate changes relative to the individuals with follow-up surveys, we compared their prepandemic responses on drug-use behaviors with responses from individuals who were followed up (Supplementary Table 5). Before the COVID-19 pandemic, individuals who were lost during the postpandemic period were more likely to report injection drug use [26] and had a higher injection frequency, but the rate of loss to follow-up did not differ by injection risk trajectories (Supplementary Table 6). To incorporate the uncertainty of behavioral changes by those lost to follow-up, we created 3 scenarios (Supplementary Table 7) where the participants lost to postpandemic follow-up (1) changed their behaviors in the same direction and magnitude as the retained cohort (reduced risk); (2) did not change their drug-use behaviors (consistent risk); or (3) increased risky behaviors by the same prepandemic multipliers relative to those who remained in follow-up (increased risk). Considering all 3 risk categories gave us a range of prevalence and incidence output that could reasonably cover the bias due to lossesto follow-up. Including changesin the drug-use network and injecting behaviors with service disruptions resulted in significantly lower prevalence and incidence of HCV and HIV ($P < .0$ Figure 4). The mean HCV prevalence in 2023 was estimated to be between 35.3% (95% CI, 35.1%–35.5%) and 43.2% (95% CI, 43.0–43.3%); the mean HIV prevalence was between 19.9% (95% CI, 19.8%–20.0%) and 24.2% (95% CI, 24.0%–24.3%)Both estimated prevalenceswere

consistently lower than those considering only service disruptions ($P < .05$). HCV incidence in 2020 had a wide range between 5.42 (95% CI, 5.35–5.50) and 11.06 (95% CI, 10.94–11.17) per 100 PY, while the incidence in 2023 was consistently lower than both baseline and service disruption-only scenarios, that is between 4.25 (95% CI, 4.18–4.33) and 7.31 (95% CI, 7.19–7.43) per 100 PY. HIV incidence followed similar patterns, with 2020 incidence between 1.31 (95% CI, 1.27–1.34) and 3.30 (95% CI, 3.23–3.37) per 100 PY, and 2023 incidence between 0.81 (95% CI, .77–.84) and 1.73 (95% CI, 1.68–1.78) per 100 PY. Our results were roughly consistent with the linear trends of active HCV/HIV prevalence within the ALIVE cohort (Supplementary Figure 1).

DISCUSSION

Using rich behavioral data from a cohort of PWID in a high-burden urban setting combined with an individual-based model, we investigated the impact of pandemic-induced changes in injecting behaviors and service disruptions on HCV and HIV transmission. As in other studies [13, 19, 20, 22], we found that disruptions in harm-reduction and clinical services during the pandemic can increase HCV (by 1.5%) and HIV prevalence (by 0.9%) by the end of 2023. However, when considering substantial and statistically significant changes in social and injecting behaviors amongst the ALIVE cohort after the pandemic, the negative impacts of service disruptions were mitigated. These results indicated that fewer PWID were actively injecting drugs. Some possible mechanisms include reduced availability of drugs or contamination of drugs with greater amounts of synthetic opioids in drug markets, as well as increased use of drugs by routes other than injection [36]. In addition, our data showed that those who continued injection drug use during the pandemic did so more frequently and within a smaller network, possibly because of declined mental health and social distancing, respectively. Interestingly, even after taking into account the lower number of injection partnerships postpandemic, the probability of syringe sharing decreased in the

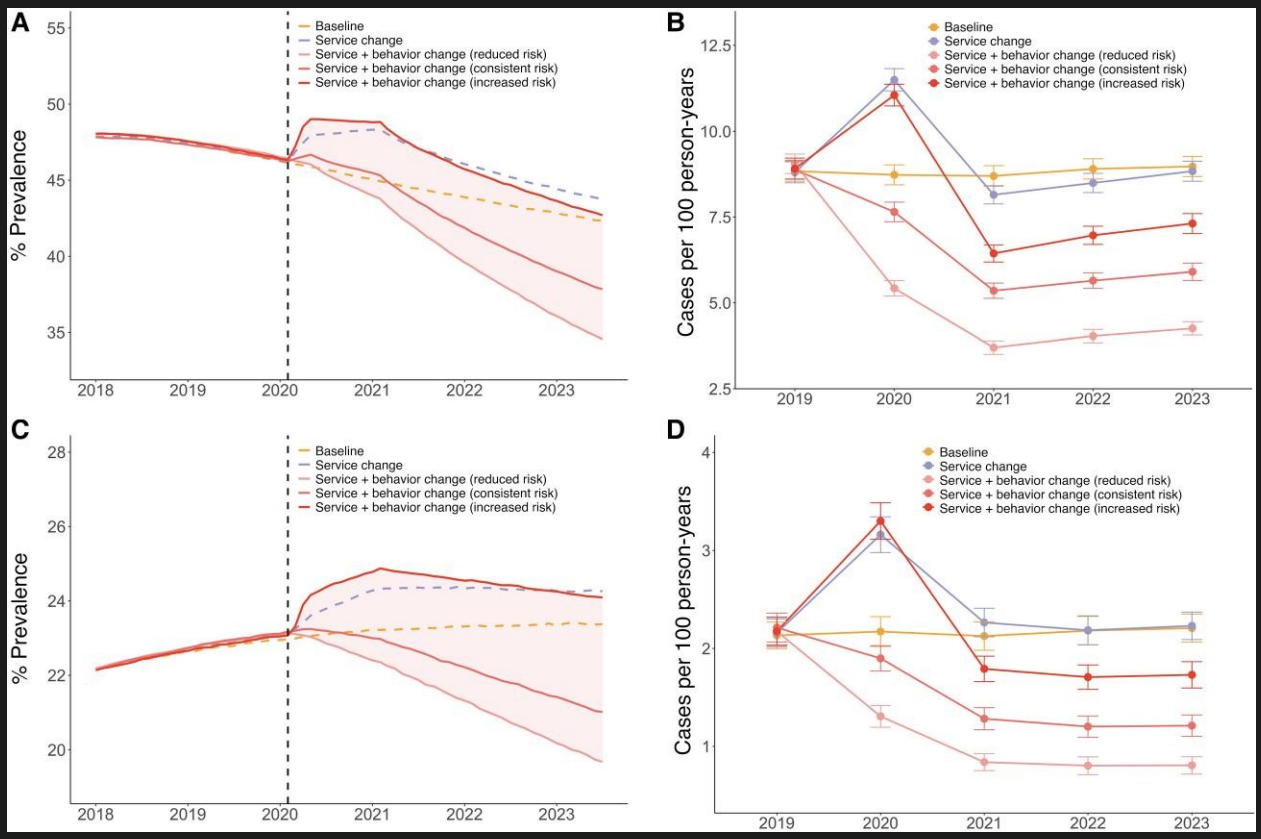

Figure 4. The estimated prevalence and incidence of HCV and HIV incorporating service and behavior changes. Prevalence and incidence of HCV (*A* and *B*) and HIV (*C* and *D*) from the beginning of COVID-19 pandemic (March 2020, vertical dashed line) to the end of latest ALIVE social network survey period (August 2023) were compared across 3 scenarios: (1) baseline scenario ("baseline," yellow) where no pandemic or subsequent responses took place; (2) service disruption-only scenario ("service change," purple) where the COVID-19 pandemic took place and clinical/harm-reduction services were disrupted in their respective durations and magnitudes as reported in Table 1; and (3) scenarios combining service disruptions and pandemic-induced behavioral changes by 3 risk levels ("service + behavior change," red) where the pandemic took place as well as service disruptions and changes in social and injecting behaviors by the ALIVE cohort. The lines and solid dots represent mean values of 200 repeated simulations; error bars represent 95% confidence intervals. Abbreviations: ALIVE, AIDS Linked to the IntraVenous Experience; COVID-19, coronavirus disease 2019; HCV, hepatitis C virus; HIV, human immunodeficiency virus.

postpandemic period despite the temporarily reduced SSP capacity that could have led to increased syringe sharing. However, these data were collected in 2022–2023, which could have missed any temporary and immediate changes in syringe sharing at the start of the COVID-19 pandemic. Simulation results suggested that considering pandemic-induced behavioral changes in addition to service disruptions could lead to significantly lower prevalence estimates by the end of 2023 (HCV by 0.9% to 8.8%; HIV by 0.1% to 4.4%).

To our knowledge, this study was the first model to include empirically informed social and injecting behavioral changes into a model of HCV and HIV transmission amongst PWID. Several studies have investigated the combined effect of service disruptions and pandemic-induced behavioral changes on sexually transmitted infections, including HIV, within the population of men who have sex with men [37, 38], with one based in Baltimore [37]. In agreement with our results, decreases in sexual partnerships due to COVID-19–related sexual distancing could potentially offset the impact of HIV clinical service closure. Although the magnitudes of behavioral changes in the above studies were hypothetical, they emphasized the substantial impact of social distancing amongst high-risk populations during the pandemic and validated our model estimates. In addition, our estimated range of HIV incidence from 2018 to 2022, after incorporating behavioral changes, was similar to the observed nonincreasing trend of HIV incidence from the CDC 2018–2022 HIV surveillance report [39], further emphasizing the significance of incorporating realistic behavioral factors into a model.

While we quantified behavior changes using detailed survey data from the ALIVE cohort, this only represented a single urban, high-burden population. Moreover, the ALIVE study is an aging cohort, despite ongoing enrollment, and may not be reflective of newly initiating PWID. Furthermore, egocentric injecting partnership data were limited, thus any sociometric or geographic clusters that could potentially alter disease transmission dynamics were not considered here. Although selection bias may be present in those participants who were included in postpandemic surveys, with potentially differential demographic, social, and behavioral characteristics, compared to those lost to follow-up, we leveraged prepandemic data to predict the pandemic-induced changes in risky behaviors amongst those lost to postpandemic follow-ups, while also creating different scenarios to account for possible behavioral patterns of this untracked population. In addition, there were temporal gaps in the postpandemic survey data (started in June 2022) that may have missed any immediate changes at the start of the pandemic. Lastly, while predicting a low likelihood of HCV/HIV outbreak, our model did not explicitly estimate risks of other important outcomes such as fatal and nonfatal overdose, and is likely to overestimate disease burdens. Risk factors observed in our study, including injecting alone, high injecting frequency, and limited access to harm-reduction services, could lead to high overdose rate and overdose mortality [40]. In previous work, while the probability of reporting an overdose by an average ALIVE participant has increased since the COVID-19 pandemic, decreases in both injection and noninjection drug use were also observed [26], hence the impact of overdose on our model results is likely limited. Additional research to understand the impact of overdose on this population is necessary given the increases in mortality observed nationally that persisted through the pandemic [41].

In conclusion, our study highlighted the importance of considering behavioral data when modeling transmission dynamics in populations such as PWID. While our study provided a potential explanation for the gap between previous concerns about service disruptions and the lack of reports on observed HCV/HIV outbreaks in the United States, the possibility of future resurgence of HCV/HIV transmission remains, particularly if behavior changes were not sustained. Disease burdens in locations that are high-risk or had recent outbreaks [42] should still be closely monitored in case of behavioral rebounds or long-term impacts of other socioeconomic factors such as homelessness and unemployment [24, 43].

Supplementary Data

Supplementary materials are available at *The Journal of Infectious Diseases* online (http://jid.oxfordjournals.org/). Supplementary materials consist of data provided by the author that are published to benefit the reader. The posted materials are not copyedited. The contents of all supplementary data are the sole responsibility of the authors. Questions or messages regarding errors should be addressed to the author.

Notes

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Author contributions. J. W., B. L. G., and A. W. conceived the project and wrote the manuscript. J. W. and A. W. performed the quantitative analysis. B. L. G., S. H. M., and G. D. K. designed and carried out the cohort study. J. W., B. L. G., K. G., and A. W. interpreted the findings. J. W., B. L. G., K. F., G. D. K., S. H. M., K. G., and A. W. interpreted the findings as well as reviewed and revised the manuscript.

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Potential conflicts of interest. All authors: No reported conflicts. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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