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HIV-1 transmission dynamics among people who inject drugs on the US/Mexico border during the COVID-19 pandemic: a prosepective cohort study

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Summary

Background We examined HIV prevalence and transmission dynamics among people who inject drugs in the U.S./Mexico border region during the COVID-19 pandemic.

Methods People who inject drugs aged ≥18 years from 3 groups were recruited: people who inject drugs who live in San Diego (SD) and engaged in cross-border drug use in Tijuana, Mexico (SD CBDUs), and people who inject drugs in SD and Tijuana (TJ) who did not engage in cross-border drug use (NCBDUs). We computed HIV prevalence at baseline and bivariate incidence-density rates (IR) at 18-month follow-up. Bayesian phylogenetic analysis was used to identify local transmission clusters, estimate their age, and effective reproductive number (Re) over time within the clusters.

Findings At baseline (n = 612), 26% of participants were female, 9% engaged in sex work, and HIV prevalence was 8% (4% SD CBDU, 4% SD NCBDU, 16% TJ NCBDU). Nine HIV seroconversions occurred over 18 months, IR: 1.357 per 100 person-years (95% CI: 0.470, 2.243); 7 in TJ NCBDU and 2 in SD CBDU. Out of 16 identified phylogenetic clusters, 9 (56%) had sequences from both the U.S. and Mexico (mixed-country). The age of three youngest mixed-country dyads (2018–2021) overlapped with the COVID-related US-Mexico border closure in 2020. One large mixed-country cluster (N = 15) continued to grow during the border closure (Re = 4.8, 95% Highest Posterior Density (HPD) 1.5–9.1) with 47% engaging in sex work.

Interpretation Amidst the COVID-19 pandemic and the border closure, cross-border HIV clusters grew. Efforts to end the HIV epidemic in the U.S. should take into account cross-border HIV-1 transmission from Tijuana. Mobile harm reduction services and coordination with municipal HIV programs to initiate anti-retroviral therapy and pre-exposure prophylaxis are needed to reduce transmission.

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Keywords: HIV; Cross-border transmission; Tijuana; Phylodynamics; People who inject drugs

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Research in context

Evidence before this study

In preparation for this study, which focuses on the dynamics of HIV transmission among people who inject drugs on the US/Mexico Border during the COVID-19 pandemic, we initiated our research by analyzing publications from the past two decades that specifically address the HIV epidemics at the San Diego-Tijuana border.[1–10] We reviewed articles from PubMed using the following keywords between 2010 and 2023: "HIV Testing; Longitudinal studies; Incidence; Substance Abuse, Intravenous; Genotype; HIV Seropositivity; Mexico". We found 15 articles across all domains. The articles demonstrate the significant role played by high-risk populations, including individuals who inject drugs, and human mobility as central drivers of local HIV epidemics in Tijuana, Mexico, and that the COVID-19 pandemic, along with preventive measures such as border closures, may have resulted in diminished access to services and an oversupply of drugs in Tijuana, leading to the disruption of drug treatment and syringe service programs in both the U.S. and Tijuana. However, no previously published work described the effect of the border closure on the HIV transmission in the area.

Added value of this study

Previous literature underscores the imperative to investigate the repercussions of the COVID-19 pandemic and border closures on local HIV transmission. Specifically, our hypothesis posits that the border closure did not disrupt existing cross-border transmission networks. We add to the literature by using phylodynamic models. Our study showed that despite border closure, persons with HIV living in San Diego still crossed into Tijuana to use drugs, suggesting that closing borders is not adequate to prevent cross-border transmission of disease or CBDU, and the growth of local clusters suggests that the disruption of harm reduction and substance use treatment services due to the COVID-19 pandemic may have in fact exacerbated cross-border HIV-1 transmission.

Implications of all the available evidence

Our study concludes that in conjunction with previous literature, it is clear that facilitating access to harm reduction and substance use treatment services in Tijuana through multi-national collaboration is urgently needed. Efforts to end the HIV epidemic in the U.S. should take into account cross-border HIV-1 transmission between Tijuana and San Diego. People who engage in CBDU may be critical to engage in HIV-1 risk reduction interventions as they are situated in growing HIV-1 molecular clusters that include residents from both sides of the border.

Introduction

People who inject drugs are vulnerable to HIV-1 infection, and their mobility across geographic borders to use injection drugs can increase their risk of exposure.[1,2] The San Ysidro Port of Entry, which separates San Diego, California, United States (U.S.), and Tijuana, Baja California, Mexico, is the busiest land border crossing in the Western Hemisphere. This crossing is a major drug trafficking route whereby heroin, fentanyl, methamphetamine, and cocaine are trafficked from Mexico to the U.S.[3] Small amounts of drugs have been partially decriminalized in Mexico since 2009 for personal consumption, and drugs are perceived to be cheaper and more widely available in Tijuana compared to the U.S.[4,5] Tijuana has a *zona roja* where sex work is legal[4,5]; in this region, cross-border drug use (CBDU) and cross-border sex are major drivers of bidirectional cross-border mobility[6] and are linked to potential HIV-1 risk behaviors such as sharing injection drug paraphernalia and paying for sex.

Over the last two decades, HIV-1 prevalence has been relatively low among people who inject drugs in both San Diego and Tijuana (estimated at 4–10%)[7–9] although HIV-1 incidence among women who inject drugs has been estimated at 2.6 per 100 person-years.[10,11] Due to cross-border mobility, HIV-1 transmission clusters have been detected involving residents on both sides of the border.[12] These clusters are more likely to include people who inject drugs, cisgender women, and heterosexuals.[12] Historically, extensive HIV-1 viral exchange between Tijuana and San Diego occurred from San Diego to Tijuana[12]; however, evidence suggests that the direction reversed during 2006–2013 with viral migration now being predominantly from Tijuana toward San Diego.[12]

Between March 21, 2020 and November 8, 2021, the U.S. and Mexico suspended all non-essential travel (i.e., tourism and recreational travel) across their borders, including the border between San Diego and Tijuana, due to the COVID-19 pandemic.[13] This closure was primarily northbound into the U.S. and posed a potential structural HIV risk due to its impact on drug availability and access to prevention services.[14] This border closure and subsequent loss of access to services may have caused a surplus of drugs in Tijuana leading to future CBDU and also disrupted drug treatment and syringe service programs in both the U.S. and Tijuana.[15,16] HIV prevention services such as needle exchange or substitution therapy programs were also disrupted on both sides of the border, but more substantially in Tijuana.[14–17] As a result, we hypothesized that the border closure and CBDU during the COVID-19 pandemic could have increased HIV transmission risk.

Changes in HIV transmission dynamics over time can be studied using molecular epidemiology methods. The HIV effective reproductive number (R_e, the average number of persons that an infected person transmits HIV to over the course of their infection during an ongoing epidemic, as opposed to the entire population being susceptible) can be inferred from HIV genetic sequences, and can further be used to evaluate the effect of interventions or policy measures on HIV transmission dynamics in people who inject drugs.[18,19]

We evaluated HIV-1 prevalence, HIV-1 incidence, and associated transmission dynamics, to characterize HIV-1 vulnerability among PWID along the U.S./Mexico border during the COVID-19 pandemic.

Methods

Setting

The study took place on the U.S./Mexico border between San Diego County, California, USA (population ~3 million people) and Tijuana Municipality, Baja California, Mexico (population ~1.9 million).[20,21]

Study population

In both cities, participants were recruited for the baseline sample collection between October 28, 2020, and October 5, 2021, via street outreach as previously described.[22] A short screener was used to identify participants who were eligible for study participation. Eligible participants were required to be aged ≥18 years or older, report injecting drugs within the last month (as evidenced through injection stigmata), and report living in San Diego County or Tijuana. We sought to enroll participants residing in San Diego who reported having crossed the border to inject drugs in Tijuana within the last two years (SD cross-border drug use [CBDU]) as well as those from either city who reported not having used illicit drugs on the other side of the border: residing either in San Diego (SD Non-cross-border drug use [NCBDU]), or Tijuana (TJ NCBDU).

Study visits

Following consent, participants were administered a behavioral questionnaire by an interviewer using computer-assisted personal interviewing and provided a blood sample at baseline. Surveys and samples were provided by participants at follow-up visits every 6 months post-baseline. Participants completed their 18-month visit between May 13, 2022 and April 17, 2023.

HIV-1 serology and partial pol sequencing

Samples obtained via whole blood with DNAGard® solution (Smith lab) underwent HIV-1 serology and sequencing at baseline and every 6-month follow-up visit. Rapid HIV-1 tests were conducted using the Miriad® HIV-1 Antibody InTec Rapid Anti-HCV Test (Avantor, PA, USA). Reactive and indeterminate tests underwent a second rapid test with Oraquick® HIV-1 (Orasure, PA, USA). Bulk sequencing of the partial HIV-1 *pol* coding region (HXB2 position 2712–3227) was performed using Viroseq v.2.0 (Selera Diagnostics, CA < USA). Sequencing was conducted by the San Diego Center for AIDS Research (CFAR) Genomics and Sequencing and Translational Virology Core.

Phylodynamic analysis

To identify HIV-1 transmission clusters that included participants from our cohort, we first reconstructed time-calibrated phylogenetic trees using HIV-1 sequences obtained within this study and a reference dataset of 80 HIV-1 partial *pol* sequences from California, USA (n = 50), and Baja California and Mexico City, Mexico (n = 30), using BEASTv1.10.4.[23] Representative HIV-1 subtype B background sequences were selected using BLAST[24] to identify the closely related genomes from California, U.S. and Mexico. Only the country of origin and sampling date were available for the reference dataset. We included all baseline sequences and, in case of individuals who seroconverted during the study period, follow up sequences. If an individual had HIV sequences obtained at baseline and at follow-up, only the first (baseline) sequence was used in the analysis. The date used for phylodynamic analysis is the sample collection date as is a requirement for phylodynamic studies[25] since it corresponds to the evolutionary timeline of the specimen used to infer the lengths of branches on the time-calibrated phylogenies. We applied Bayesian skyline plot models to characterize changes in the effective population size of the studied population,[26] with an HKY nucleotide substitution model with gamma-distributed rate variation among sites (HKY + G), and a lognormal relaxed molecular clock model with a lognormal prior on the mean parameter and a normal prior on the standard deviation parameter. We ran Markov chain Monte Carlo (MCMC) for 1×10^8 iterations (with 10% removed as burn-in before the MCMC reached equilibrium). We then used the obtained tree distribution to identify HIV-1 transmission clusters defined as the largest clades that include individuals from our study and have a posterior probability support of ≥90%. "Large" clusters were defined as those that include 10 sequences.

To describe changes in HIV-1 transmission dynamics within the two largest identified clusters before and after the COVID-related border closure, we applied Bayesian birth-death skyline (BDSKY) model[27] and estimated changes in the R_e over time for both clusters separately using BEAST2.[28] BDSKY model assumes that lineages are added to the tree upon infection (a "birth" event (transmission event)) and are removed upon becoming noninfectious (a "death" event which can correspond to getting treatment, dying, or moving away from the studied population in the case of HIV transmission). For each cluster, we parameterized the

BDSKY model so that the R_e changed as a piecewise constant function through time at five pre-specified intervals: 1) before the emergence of the cluster; 2) between the emergence of the cluster and January 2013; 3) January 2013–January 2018; 4) January 2018–January 2020; 5) January 2020–October 2021 for cluster 1 and January 2020–July 2021 (date of the last sampling event in each cluster). We chose these intervals to cover the period of border closure and the equivalent period of time preceding the border closure. For the large cluster 1 analysis, the sampling proportion was kept zero before January 2020 (since all individuals in the cluster were cohort participants); after that it was informed with a beta prior (alpha = 1, beta = 10). For the large cluster 2 analysis, the sampling proportion was kept constant throughout the time with the same prior as for the cluster 1. Becoming uninfectious rate was kept constant over time (with a lognormal prior with mean = 0.0 and standard deviation = 1.0) since we do not have reason to believe that duration of infectivity changed over time in the studied area. We ran BDSKY Markov chain Monte Carlo (MCMC) for 3×10^7 iterations (with 10% removed as burn-in).

Statistical analysis

HIV-1 prevalence, bivariate HIV-1 incidence-density rates, and exact 95% confidence intervals (CI) were calculated by participant characteristics between baseline and the 18-month follow-up visit. Person years (PY) were calculated for the time between visits based on seroconversion, assuming the seroconversion occurred at the midpoint between visits. Participant characteristics included demographics, CBDU status, and HIV-1 associated behaviors. Both incidence rate ratio (IRR) and incidence rate difference (IDD) were calculated to compare HIV-1 incidence-density rates across participant characteristics; only IDD was reported when the seroconversions in a particular group were 0.[29] Sensitivity analyses were conducted to account for loss to follow-up. We calculated upper and lower boundary incidence-density rates using exact 95% confidence intervals (CIs) assuming that all lost to follow-up could have seroconverted (upper boundary) and none of the lost to follow-up seroconverted (lower boundary). To assess whether different pandemic stages impacted recruitment (and therefore result interpretation), we examined the rate of recruitment by restrictive periods in San Diego and Tijuana during our data collection period.

Ethics statement

Protocols were approved by institutional review boards at the University of California San Diego and Xochicalco University. All participants provided written informed consent. Each participant received $20 USD for their time for participation in the baseline visit, and $20 USD for each 6-month visit.

Role of the funding source

The funders did not have any role in the study design, data collection, analysis, interpretation, or writing of the report.

All items in the STROBE checklist were included.

Results

Among 612 participants at baseline, the median age was 43 years (IQR 35, 52), median age at first injection was 20 years (IQR 17, 26), and most identified as cisgender men (74%; 449/612) and Latinx/Hispanic/Mexican (72%; 440/612) (Table 1). Approximately 1% of participants (5/612) identified as non-cisgender, 9% (54/612) reported exchange sex in the past 6 months, and 52% (317/612) reported receptive syringe sharing in the past 6 months. HIV-1 prevalence at baseline was 8% (49/612), and, although not statistically significant, differed by sample/study group [SD CBDU = 8/206 (4%), SD NCBDU = 9/204 (4%), TJ NCBDU = 32/202 (16%)]. Of the participants who returned for their 18-month follow-up visit and were tested for HIV-1, there were 9 seroconversions during 663.40 PY of follow-up for an incidence rate of 1.36 (95% CI: 0.47, 2.24). Two seroconversions occurred among the SD CBDU group (Incidence Rate [IR]) (0.76 [95% CI 0.00, 1.80]), seven among the TJ NCBDU group (2.88 [0.75, 5.02]), and none among SD NCBDU. When comparing incidence rates across the study groups, HIV-1 incidence was significantly higher among TJ NCBDU relative to SD NCBDU, IDD: 0.03 (95% CI 0.00, 0.06), p-value = 0.03. HIV-1 incidence among TJ NCBDU participants was also notably higher than SD CBDU participants, although only marginally significant [IRR: 3.82 (0.79, 18.38), p-value = 0.0948; IDD: 2.12 (–0.2597, 4.5061), p-value = 0.0795]. HIV-1 incidence varied by gender and sexual orientation. HIV-1 incidence was 2.36 (0.05, 4.67) among cisgender women, 0.82 (0.02, 1.62) among cisgender men, 21.77 (0.00, 64.45) among participants identifying as transgender/non-binary, 1.23 (0.38, 2.08) among those who identified as heterosexual and 7.90 (0.00, 23.38) among those who identified as lesbian, gay, or bisexual. All seroconversions occurred within the first 6 months of the study period. Additional information can be found in Table 2.

Twenty-eight percent (28%; 251) of HIV-1 negative participants at baseline were lost to follow-up. Loss to follow-up was more common among SD NCBDU, younger participants, non- Latinx/Hispanic/Mexican participants, and those who did not report sex work. The sensitivity analyses assessing loss to follow-up showed an incidence rate assuming none of the participants who were lost to follow-up seroconverted over 18-months of 1.14 (0.39, 1.88), and an incidence rate assuming all who were lost to follow-up seroconverted over 18-months as, 21.48 (18.25, 24.71) (Supplementary Table S1).

Characteristic	San Diego CBDU (n = 206)	San Diego NCBDU (n = 204)	Tijuana NCBDU (n = 202)	Total (n = 612)
Age, Median (IQR)	41 (35, 51)	41 (31, 53)	44 (38, 52)	43 (35, 52)
Cisgender woman, n (%)	44 (21%)	58 (28%)	55 (27%)	157 (26%)
Cisgender man, n (%)	161 (78%)	146 (72%)	142 (70%)	449 (73%)
Trans/non-binary/other, n (%)	1 (<1%)	0	4 (2%)	5 (1%)
Hispanic/Latinx/Mexican, n (%)	156 (76%)	89 (44%)	195 (97%)	440 (72%)
Age at first injection, Median (IQR)	20 (17, 25)	21 (17, 27)	20 (17, 26)	20 (17, 26)
Exchange sex (past 6 months)	13 (59%)	6 (67%)	35 (73%)	54 (9%)
Receptive Syringe Sharing in past 6 months	95 (46%)	83 (41%)	139 (69%)	317 (52%)
HIV prevalence	8 (4%)	9 (4%)	32 (16%)	49 (8%)

IQR = InterQuartile range; CBDU = Cross-border drug use; NCBDU = Non-cross-border drug use.

Table 1: **Baseline characteristics, La Frontera Cohort, San Diego, USA & Tijuana, Mexico (n = 612).**

HIV-1 phylodynamic analysis

We used the time-calibrated phylogenetic tree to identify local transmission clusters that include sequences from our study (referred to as cohort sequences throughout). We were able to sequence 45 of the 49 people living with HIV at baseline (not all sequences were high quality), and 40 belonged to clusters. We identified 16 clusters that included at least 1 cohort sequence (cluster size range 2–17) (Fig. 1); out of those, 2 clusters were large (N = 15 for large cluster 1 and N = 17 for large cluster 2). Of the 16 identified clusters, only 7 had sequences from one country (5 clusters had U.S. sequences only and 2 clusters had Mexico sequences only), while 9 clusters had sequences from both the U.S. and Mexico, indicating frequent viral mixing between the two countries. The U.S. only clusters each had 1 cohort sequence each; 4 with one SD NCBDU and 1 with one SD CBDU. The analysis shows no significant difference in the rate of interview count per months in the restrictive period vs. the unrestricted period.

Both large clusters included sequences from both the U.S. and Mexico. Large Cluster 1 consisted of 4

	Population	HIV seroconversions	Person-years (PY) at risk	Incidence rate (95% CI) per 100 person-years
Overall	Overall	9	663.40	1.357 (0.470, 2.243)
Sample	San Diego, CBDU	2	264.82	0.755 (0.000, 1.802)
	San Diego, NCBDU	0	155.77	0 (0,0)
	Tijuana, NCBDU	7	242.81	2.883 (0.747, 5.019)
City	San Diego	2	420.591	0.476 (0.000, 1.135)
	Tijuana	7	242.812	2.883 (0.747, 5.019)
Race	White	1	233.645	0.428 (0.000, 1.267)
	Black	0	25.251	0 (0, 0)
	Asian/Native Hawaiian/Pacific Islander	0	7.934	0 (0, 0)
	Indigenous/American Indian/Alaskan Native	1	211.172	8.951 (0.000, 26.495)
	Multi-racial	4	76.656	5.218 (0.104,10.332)
	Other race	3	305.845	0.981 (0.000, 2.091)
Age	≤40	4	260.753	1.534 (0.031, 3.037)
	>40	5	402.650	1.242 (0.153, 2.330)
Gender	Man	4	489.158	0.018 (0.016, 1.619)
	Woman	4	169.652	2.358 (0.047, 4.668)
	Trans/non-binary/other[a]	1	4.593	21.773 (0.000, 64.449)
Sexual identity	Heterosexual	8	650.742	1.229 (0.377, 2.081)
	Lesbian, gay, or bisexual	1	12.661	7.898 (0.000, 23.379)
Exchange sex (past 6 months)	Yes	4	217.759	1.837 (0.037, 3.637)
	No	5	445.644	1.122 (0.139, 2.105)
Receptive syringe sharing (past 6 months)	Yes, ever	4	151.532	2.640 (0.053, 5.227)
	No, never	5	511.871	0.977 (0.121, 1.833)

CBDU = Cross-border drug use; NCBDU = Non-cross-border drug use. [a]n = 5.

Table 2: **HIV incidence by participant characteristic among 563 people who inject drugs (PWID) over 18-months LA FRONTERA cohort, San Diego, USA & Tijuana, Mexico.**

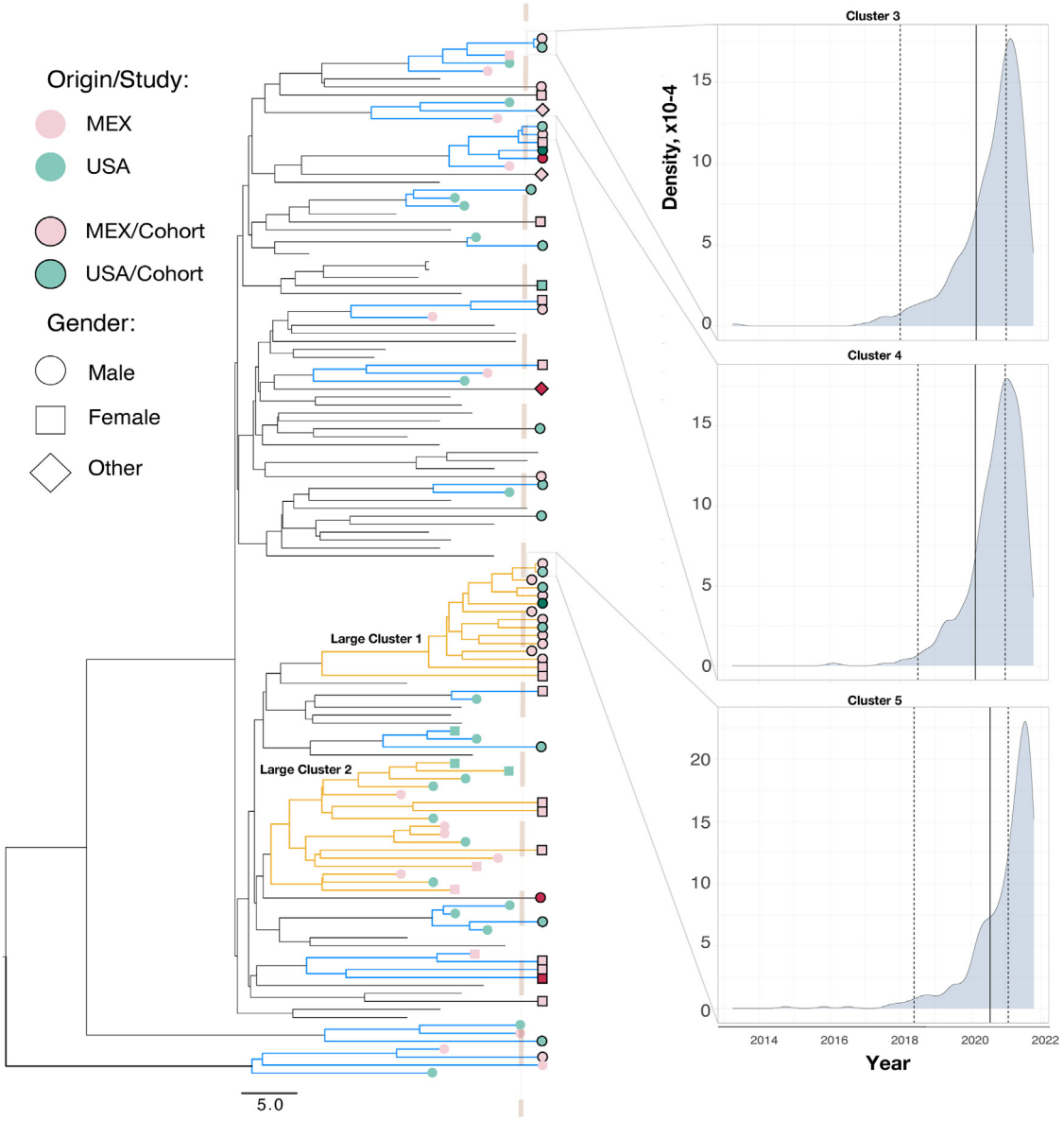

Fig. 1: Molecular clock tree reconstructed from 45 baseline and 6 seroconversion sequences from La Frontera cohort and 80 background sequences from San Diego and Mexico (left) and time to the most common recent ancestor (tMRCA) posterior densities of the 3 recent cross border clusters (right). Left panel: Pink and green tips depict sequences from individuals from Mexico and the United States (US) respectively; tips with black stroke indicate cohort sequences; tips in darker pink and green color represent study seroconverters. All clusters with posterior probability support ≥ 90% and including at least one cohort sequence are marked in blue; the two large clusters are marked in yellow. The three most recent cross-border transmission clusters and their respective tMRCA posterior densities are shown on the right panel. In the left panel, the bar at the bottom indicates the scale of the tree in years. In the right panel, the solid line represents the median TMRCA estimate and the dotted lines represent 95% HPD intervals.

sequences from the U.S. (27%; 4/15) all of whom were from SD CBDU, and 11 from Mexico (73%; 11/15) who were TJ NCBDU. Large Cluster 1 was predominantly male (87%; 13/15), and 47% (7/15) of cohort participants in the cluster reported sex work (6 males and 1 female). One sequence in large Cluster 1 was from a cohort SD CBDU participant who seroconverted. Large Cluster 2 consisted of 7 sequences from the U.S. (41%; 7/16) and 10 from Mexico (59%; 10/16). There were 3 cohort sequences, all of which were females TJ NCBDU who reported sex work.

Among the other 14 clusters, 3 clusters were recent (i.e., their time to most recent comment ancestor (TMRCA) Highest Posterior Densities (HPDs) overlapped with the US-Mexico border closure in 2020). Specifically, cluster 3 TMRCA was estimated to be in March, 2020 (August 2018–January 2021); cluster 4 TMRCA – November 2019 (February 2018–January 2021); and cluster 5 TMRCA – December 2019 (April 2018–January 2021). All of the recent clusters only included 2 sequences, one from the U.S. and Mexico each. Large Cluster 1 included cohort sequences only (N = 15) and its TMRCA was estimated to be in December 1996 (95% Highest Posterior Density (HPD) May 1990–October 2002); Large Cluster 2 included 3 cohort sequences (N = 17) and its TMRCA was estimated to be in October 1993 (95% Highest Posterior Density (HPD) January 1988–April 1999).

R_e estimation

We estimated R_e changes over time for both large clusters (Fig. 2) to describe transmission dynamics along the US-Mexico border. For the large cluster 1, the only period when the R_e was estimated to be statistically significantly above 1 was the period during the pandemic and the US-Mexico border closure (January 2020–October 2021); at that time the R_e was estimated to be 4.8 (95% HPD 1.5–9.1). For the large cluster 2, the only period when the cluster was growing was the period close to the cluster's TMRCA up until early 2013: the R_e was estimated to be 2.1 (95% HPD 1.1–3.7) then. In more recent years, the R_e was estimated to be high but with not statistically significantly above 1 (median 3.9, 95% 0.1–8.1).

Discussion

Our analysis showed that the HIV epidemics in Tijuana and San Diego are intertwined, and that border closure did not impact frequent viral mixing between the two municipalities. Indeed, we found evidence of growth for one of the large clusters at the border (Large Cluster 1), and did not find evidence of decline for the other (Large Cluster 2). Specifically, the younger cluster (Large Cluster 1) included more men who exchange sex and grew the fastest during and after the COVID-19 border closure; while Large Cluster 2 included more women who exchange sex and peaked in growth >10 years ago. The two large growing clusters both included individuals from both sides of the border.

The disruption of harm reduction and substance use treatment services due to the COVID-19 pandemic may have exacerbated cross-border HIV-1 transmission.[14,15,30] During the pandemic in Tijuana, government sponsored housing and methadone were temporarily provided only to people who inject drugs with COVID-19 symptoms, and non-COVID-19 related medical care was inaccessible.[15] Several policies had already decreased funding to civil organizations[31] and the public healthcare system,[32] which contributed to a massive disruption in providing healthcare services in the face of the pandemic. In addition, reduced tourism from the U.S. and lockdowns drastically reduced income opportunities among people who inject drugs in Tijuana, which might

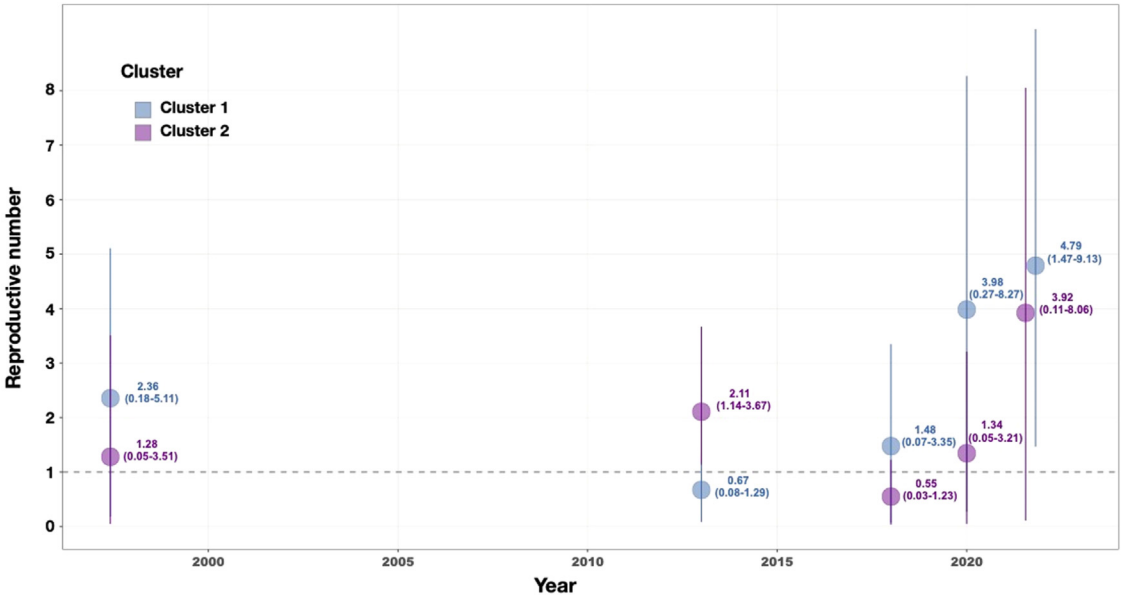

Fig. 2: Estimates of the effective reproductive number (R_e) for large cluster 1 (n = 15, in blue) and large cluster 2 (n = 17, in purple). Circles and vertical bars represent the mean and 95% HPD of the Re obtained from the BDSKY model.

have further limited access to sterile syringes and led to higher frequency of syringe sharing.[33]

While closing the San Ysidro Port of Entry northbound may have reduced CBDU, our study showed that people who inject drugs living in San Diego still crossed into Tijuana to use drugs, suggesting that closing borders is not adequate to prevent cross-border transmission of disease or CBDU. CBDU mobility was present in both existing and growing HIV-1 phylogenetic clusters. Studies on CBDU before the pandemic found that factors independently associated with injecting drugs in Mexico included being younger at first injection, injecting heroin, distributive syringe sharing, and recently transporting drugs.[34] Likewise, those who were deported from the U.S. to Tijuana were more likely to inject and share syringes with people who inject drugs from the U.S.[35]

Future interventions should address the widespread impact of the COVID-19 pandemic and related policies affecting access to health on HIV-1 incidence among CBDU in San Diego and Tijuana. At the structural level, our findings support urgently needed binational collaborations which facilitate the access of harm reduction and substance use treatment services in Tijuana. At the network level, interventions can prioritize utilizing social networks to disseminate harm reduction and HIV-1 prevention services such as information, condoms, and injection equipment, or to change social and injection network norms to discourage HIV-1 risk behaviors.[36] Such interventions should include communities of people who inject drugs on the both sides of the border. Finally, individual-level nonpharmaceutical interventions can also be considered in these resource-constrained settings.

Our study is not without limitations. First, although the HIV-1 incidence rate was high, the overall number of seroconversions was low given the eighteen-month period, limiting our ability to assess differences in incidence by participant characteristics. Likewise, incidence rates among groups with small samples should be interpreted with caution. Second, our behavioral survey relied on self-reports, which can be prone to socially desirable responding. Third, loss to follow-up was more common among SD NCBDU, younger participants, non-Latinx/Hispanic/Mexican participants, and those who did not report sex work, which may have biased our HIV-1 incidence estimates and transmission cluster characterization. Due to the high mortality of COVID-19, HIV-1, and overdose deaths among people who inject drugs (there were a substantial increase in fatal opioid overdoses in San Diego, mostly driven by fatal fentanyl overdose),[37] participants may have died from these conditions. In addition, many participants were displaced due to law enforcement. This loss to follow-up may have biased our incidence calculations. However, our sensitivity results assuming that either all participants lost to follow-up either remained uninfected (lower interval) or seroconverted (upper interval) show that our observed IR may be conservative, as the lower IR rate is similar to what was observed. Given that most participants who were lost to follow-up were experiencing negative social determinants of health, and literature shows that social determinants of health are associated with HIV incidence,[38] we believe that our observed incidence is a conservative estimate. Furthermore, our follow-up rate of 72% during a pandemic is on par with follow-up rates among PWID in non-pandemic settings.[39] Finally, the phylodynamic analysis was limited by the small number of sequences in our analysis, which resulted in wider HPD intervals.

Conclusion

Although the San Ysidro border was closed to non-essential northbound travel during the COVID-19 pandemic, HIV-1 transmission persisted, with growing clusters consisting of people who inject drugs on both sides of the border, CBDU, and people of both genders who reported exchanging sex. Our results demonstrate that efforts to end the HIV epidemic in the U.S. should take into account cross-border HIV-1 transmission from Tijuana. People who engage in CBDU may be critical to engage in HIV-1 risk reduction interventions as they are situated in HIV-1 molecular clusters that include residents from both sides of the border. In times of crisis (and beyond), mobile harm reduction services, such as those providing syringes and HIV testing, are needed on both sides of the border. Improved coordination with local HIV prevention programs would allow for more effective evidence-based substance use treatment, Antiretroviral Therapy and Pre-Exposure Prophylaxis initiation.

Contributors

Author contributions: B.S. and S.S. conceptualized the study; A.C., T.V., A.B., and C.S. designed the study; T.V. designed phylodynamic analyses; A.C. and T.V. conducted phylodynamic analyses. C.S., A.C., T.V., and B.S. analyzed the data; A.C., T.V., A.B., and C.S., A.H., and G.R. interpreted the data; CN conducted the incidence analyses; B.S. and C.S. drafted the manuscript; all authors reviewed, edited and approved the manuscript.

Data sharing statement

Data is available upon reasonable request. Please contact the corresponding authors for more information.

Declaration of interests

The authors report no conflicts of interest.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.lana.2024.100751.

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