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Correlates of Coronavirus Disease 2019 (COVID-19) Vaccine Hesitancy Among People Who Inject Drugs in the San Diego-Tijuana Border Region

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Background. People who inject drugs (PWID) are vulnerable to acquiring severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). We examined correlates of coronavirus disease 2019 (COVID-19) vaccine hesitancy among PWID in the US-Mexico border region, of whom only 7.6% had received ≥ 1 COVID-19 vaccine dose by September 2021.

Methods. Between October 2020 and September 2021, participants aged ≥ 18 years from San Diego, California, USA, and Tijuana, Baja California, Mexico, who injected drugs within the last month completed surveys and SARS-CoV-2, human immunodeficiency virus (HIV), and hepatitis C virus (HCV) serologic testing. Logistic regressions with robust standard error estimation via generalized estimating equations identified factors associated with being unsure or unwilling to receive COVID-19 vaccines.

Results. Of 393 participants, 266 (67.7%) were willing to receive COVID-19 vaccines and 127 (32.3%) were hesitant (23.4% unwilling and 8.9% unsure). Older participants, those with greater food insecurity, and those with greater concern about acquiring SARS-CoV-2 were more willing to be vaccinated. Higher numbers of chronic health conditions, having access to a smart phone or computer, and citing social media as one's most important source of COVID-19 information were independently associated with vaccine hesitancy. COVID-19-related disinformation was independently associated with vaccine hesitancy (adjusted odds ratio: 1.51 per additional conspiracy theory endorsed; 95% confidence interval: 1.31–1.74).

Conclusions. Nearly one third of people injecting drugs in the US-Mexico border region were COVID-19 vaccine hesitant, which was significantly associated with exposure to social media, disinformation and co-morbidities and inversely associated with food security and high perceived threat of COVID-19. Interventions that improve accurate knowledge of and trust in COVID-19 vaccines are needed in this vulnerable population.

Keywords. COVID-19 vaccines; disinformation; SARS-CoV-2; social media; substance use.

An ongoing contributor to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) transmission is low vaccine uptake [1]. In high-income countries, structural issues such as limited transportation and healthcare access disproportionately affect under-represented minorities and those with low socio-economic status [2]. Coronavirus disease 2019 (COVID-19) vaccine hesitancy has also emerged as a major problem, due at least in part to an "infodemic" of misinformation and disinformation [3]. Misinformation refers to inaccurate information shared without malicious intent, whereas disinformation is the deliberate spread of false information, for example, through organized social media campaigns [4]. Although both misinformation and disinformation have sowed confusion about the epidemiology of SARS-CoV-2 and illness severity [3], disinformation campaigns have seriously undermined public confidence in COVID-19 vaccine safety in the United States and elsewhere [5, 6], especially among people who are Black and Latinx [7].

People who use drugs, especially people who inject drugs (PWID), may be especially vulnerable to SARS-CoV-2 infection due to exposures such as using drugs with others, engaging in sex work [8], elevated prevalence of chronic diseases [9], homelessness, incarceration [8, 10], and other structural factors that limit healthcare engagement such as stigma [11].

We previously reported that over one third of PWID in San Diego County and Tijuana, Mexico, had been infected with SARS-CoV-2, and only 9% had received at least 1 COVID-19 vaccine dose [8]. Herein we studied COVID-19 vaccine hesitancy in the same population, hypothesizing that

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socio-structural factors such as homelessness and Latinx ethnicity would be significantly associated with COVID-19 vaccine hesitancy, as well as COVID-19 misinformation. We were also interested in studying whether exposure to COVID-19 disinformation was significantly associated with COVID-19 vaccine hesitancy in a population that has historically had limited access to social media [12].

METHODS

Participants and Eligibility

Between 28 October 2020 and 10 September 2021, street outreach was used to recruit participants aged ≥ 18 or older who injected drugs within the last month and reported living in San Diego County or Tijuana, as previously described [8]. Participants were compensated 20 USD for study visits. Protocols were approved by institutional review boards at the University of California San Diego and Xochicalco University.

Survey Measures

After providing informed consent, participants underwent interviewer-administered surveys at baseline and approximately one week later using computer assisted personal interviews. Surveys assessed socio-demographics, substance use, chronic health conditions (eg, diabetes, asthma, hypertension), food insecurity [13], and COVID-19 experiences, exposures, and protective behaviors (eg, social distancing, masking).

To assess COVID-19 misinformation, we presented participants with seven statements about SARS-CoV-2 transmission, severity, immunity, symptoms, treatments, and vaccines, and asked them to classify each statement as "True," "False," or "Unsure." We then created a binary variable for each statement indicating whether the participant was misinformed or not.

We assessed COVID-19 disinformation through endorsement of six conspiracy theory items, three of which were based on work by Romer and Jamison (eg, "COVID-19 was created by the pharmaceutical industry" or "the Chinese government"; "childhood vaccines cause autism" [7]). Based on field experience and the media, we added 3 new items: "COVID-19 vaccines include a tracking device," "alter DNA," or are being offered to communities differentially (ie, "COVID-19 vaccines offered to 'people like me' are not as safe"). We dichotomized responses to indicate endorsement of disinformation ("True" and "Unsure") or not ("False") and summed them into a total score ranging from 0 to 6. The mean inter-item correlation value was 0.31, which indicates optimal internal consistency [14].

Our primary outcome of interest, COVID-19 vaccine hesitancy, was assessed by asking participants whether they would agree to receive a free COVID-19 vaccine. This question was introduced on 5 November 2020. However, items on COVID-19 knowledge and beliefs were not introduced until 14 May 2021.

SARS-CoV-2 Antibody Detection

Serology was conducted by Genalyte® (San Diego, California, USA), using their Maverick™ Multi-Antigen Serology Panel [15] that detects immunoglobulin G (IgG) and immunoglobulin M (IgM) antibodies to 5 SARS-CoV-2 antigens (Nucleocapsid, Spike S1-S2, Spike S1, Spike S1-RBD, Spike S2) within a multiplex format based on photonic ring resonance. A machine learning algorithm was used to call results using the Random Forest Ensemble method with 3000 decision trees [16].

HIV and HCV Serology

Rapid human immunodeficiency virus (HIV) and hepatitis C virus (HCV) tests were conducted using the Miriad® HIV/HCV Antibody InTec Rapid Anti-HCV Test (Avantor, Radnor, Pennsylvania, USA). Reactive and indeterminate tests underwent a second rapid test with Oraquick® HIV or Oraquick® HCV, respectively (Orasure, Bethlehem, Pennsylvania, USA).

Statistical Analysis

Participants who responded that they were unsure or would not agree to receive a free COVID-19 vaccine were coded as vaccine hesitant.

Characteristics of participants who were and were not COVID-19 vaccine hesitant were compared using Mann-Whitney U tests for continuous variables and χ^2 or Fisher exact tests for categorical variables.

Univariate and multivariable logistic regressions with robust standard error estimation via generalized estimating equations were performed to identify factors associated with vaccine hesitancy. Following Hosmer and Lemeshow's "purposeful selection of variables" approach to model building [17], variables attaining significance at a level of $\alpha = .10$ in the univariate regressions, were considered for inclusion in multivariable models. The final model was selected based on subject matter significance, relationships among potential predictors (eg, correlations, confounding, and interactions) and statistical significance retaining. Only variables retaining significance levels at $\alpha = 0.05$ level were included in the final model. The multivariable model also controlled for time using a linear and quadratic term, which were highly significant but did not change the parameter estimates or their significance. We checked the final multivariable model for integrity by assessing relationships between the predictors (eg, correlations, confounding, interactions). Multi-collinearity was assessed and ruled out by appropriate values of the largest condition index and variance inflation factors. All statistical analyses were conducted using SAS, version 9.4.

RESULTS

Sample Characteristics and Vaccine Hesitancy

Of 550 participants who completed baseline and supplemental interviews, 508 (92.4%) reported that they were not vaccinated.

Of these, 393 (77%) had been asked the vaccine hesitancy and COVID-19 knowledge questions and were included in this analysis. Of these 393 participants, most identified as male (74.6%) and Hispanic, Latinx, or Mexican (81.4%), and by design, approximately half (48.6%) resided in San Diego County (Table 1). Mean age was 42.4 years (standard deviation [SD]: 10.2).

In the past 6 months, most participants (90.6%) injected either heroin or fentanyl, and 40.6% injected methamphetamine. Additional noninjection substance use involved smoking cigarettes (89.3%), methamphetamine (57.0%), marijuana (51.4%), and heroin or fentanyl (29.3%). Over one third were HCV-seropositive (38.9%), 8.4% were HIV-seropositive, and 33.3% reported at least 1 other chronic health condition.

Most participants reported reduced food security (83.7%) and income (70.7%) since the COVID-19 pandemic began, and 40.7% tested SARS-CoV-2 seropositive. Substantial proportions of participants reported knowing someone who had died from COVID-19 (31.0%) and knowing someone who had been vaccinated for COVID-19 (61.1%). Overall, 22.1% had access to a smart phone (19.3%) or computer (9.7%).

Of the 393 participants, 266 (67.7%) were willing to receive COVID-19 vaccines, and 127 (32.3%) were hesitant (23.4% unwilling and 8.9% unsure). Compared to those who were willing to be vaccinated against COVID-19 (Table 2), vaccine-hesitant participants were younger (mean age: 40.5 vs 43.3 years, $P = .009$) and had higher education (mean years of schooling completed: 10.1 vs 9.0, $P < .001$). Higher proportions of vaccine-hesitant participants were born in the United States (57.5% vs. 33.5%, $P < .001$), currently resided in San Diego (57.5% vs 44.4%, $P = .01$), and were homeless (51.2% vs 37.2%, $P = .009$). Compared to other participants, those who felt that they had already had COVID-19 were more likely to be vaccine-hesitant (16.5% vs 6%, $P < .001$).

Almost all participants endorsed at least 1 statement that reflected COVID-19 misinformation (99%), such as thinking that COVID-19 is about as dangerous as having the flu (63.9%). Respondents who thought COVID-19 vaccines were unsafe for pregnant women or believed they could tell if someone had COVID-19 by looking at them were significantly more likely to be vaccine hesitant.

A majority of participants also endorsed at least 1e conspiracy theory related to COVID-19 or vaccines (85%). COVID-19 disinformation scores were higher among those who were vaccine hesitant (mean number of COVID-19 conspiracy theories endorsed out of 6 total: 3.7 vs 2.4, $P < .001$). Vaccine-hesitant participants were more likely to identify social media as their primary source of COVID-19-related information (21.1% vs 8%, $P < .001$). There were no differences observed in vaccine hesitancy related to identifying friends as a primary source of COVID-19 information (50.8% overall) or ever having had a flu vaccine (45.5% overall).

COVID-19-Related Correlates of Vaccine Hesitancy

Participants who engaged in at least 1 protective behavior (eg, social distancing, isolating oneself, wearing masks, increasing handwashing) were significantly less likely to be vaccine hesitant (unadjusted odds ratio [OR]: 0.43; 95% confidence interval [CI]: .23–.81; Table 2). Those who were more worried about getting COVID-19 were also less likely to be vaccine hesitant (OR: 0.86 per point increase; 95% CI: .79–.93). Conversely, those who thought they had had COVID-19 or had been tested for COVID-19 outside of this study were significantly more likely to be vaccine hesitant, and having been exposed to somebody testing positive for COVID-19 was marginally associated with higher unadjusted odds of vaccine hesitancy (OR: 2.21; 95% CI: .96–5.06; $P = .06$). Regarding other COVID-19-related experiences and exposures, having COVID-19 symptoms on the day of the interview or knowing someone else who had been vaccinated against COVID-19 were not associated with vaccine hesitancy. Testing SARS-CoV-2 seropositive in our study was not associated with vaccine hesitancy although participants were unaware of their test results at the time of interview.

Factors Independently Associated With Vaccine Hesitancy

In our final multivariate model controlling for time (Table 3), older age was inversely associated with vaccine hesitancy (adjusted OR [aOR]: 0.97 per year increase in age; 95% CI: .95–.99). Participants with greater food insecurity and concern about acquiring SARS-CoV-2 were less likely to be vaccine hesitant (aOR: 0.44; 95% CI: .23–.87; and aOR: 0.85 per point increase; 95% CI: .77–.93, respectively). Greater numbers of chronic health conditions were independently associated with vaccine hesitancy (aOR: 1.46 per additional chronic condition; 95% CI: 1.17–1.82). Those with a smart phone or computer access were almost 4 times more likely to be vaccine hesitant (aOR: 3.75; 95% CI: 2.07–6.82). Citing social media as one's most important source of COVID-19 information was marginally associated with vaccine hesitancy (aOR: 1.86; 95% CI: .94–3.70, $P = .07$). Finally, COVID-19-related disinformation was independently associated with vaccine hesitancy (aOR: 1.51 per additional conspiracy theory endorsed; 95% CI: 1.31–1.74).

In a sub-analysis that included the 42 participants who reported having had at least 1 COVID-19 vaccine dose and coded them as willing, parameter estimates in our final model were essentially unchanged, with the exception of primarily obtaining COVID-19 information from social media, which became highly significant.

DISCUSSION

Vaccine hesitancy is a critical challenge to COVID-19 pandemic control efforts, especially for vulnerable populations including people who use and inject drugs. In our community-based sample of PWID in the San Diego-Tijuana border region, nearly

Table 1. Characteristics Associated With COVID-19 Vaccine Hesitancy Among PWID in San Diego, California, USA, and Tijuana, Mexico (N = 393)

Baseline Characteristics	Vaccine Hesitant N = 127	Not Vaccine Hesitant N = 266	Total N = 393	*P*
Sociodemographics				
Male	95 (74.8%)	198 (74.4%)	293 (74.6%)	.94
Mean age (SD)	40.5 (10.8)	43.3 (9.8)	42.4 (10.2)	.009
Hispanic/Latinx/Mexican	94 (74.0%)	226 (85.0%)	320 (81.4%)	.009
Speaks English	91 (71.7%)	164 (61.7%)	255 (64.9%)	.05
Born in the USA	73 (57.5%)	89 (33.5%)	162 (41.2%)	<.001
Primary residence in San Diego	73 (57.5%)	118 (44.4%)	191 (48.6%)	.02
Mean years of school completed (SD)	10.1 (3.0)	9.0 (3.4)	9.3 (3.3)	<.001
Married or common law	26 (20.5%)	57 (21.4%)	83 (21.1%)	.83
Average monthly income < 500 USD	86 (67.7%)	165 (62.0%)	251 (63.9%)	.27
Has a smart phone or access to a computer	51 (40.2%)	36 (13.5%)	87 (22.1%)	<.001
Potential COVID-19 exposures				
Homeless[a]	65 (51.2%)	99 (37.2%)	164 (41.7%)	.009
Mean no. of hours spent on the street (SD)[a]	16.7 (7.6)	14.7 (6.9)	15.3 (7.2)	.008
Incarcerated[a]	10 (7.9%)	20 (7.5%)	30 (7.6%)	1.00
Mean no. of people in the same household (SD)[a]	6.2 (15.2)	5.9 (11.9)	6.0 (13.0)	.04
Engaged in sex work[a]	15 (11.8%)	40 (15.0%)	55 (14.0%)	.39
Client of sex worker[a]	6 (4.7%)	19 (7.1%)	25 (6.4%)	.51
Exposed to someone diagnosed with COVID-19	12 (9.4%)	12 (4.5%)	24 (6.1%)	.06
Income worse since COVID began	78 (61.9%)	197 (74.9%)	275 (70.7%)	.008
Low/very low food security since COVID began	98 (77.2%)	231 (86.8%)	329 (83.7%)	.02
Substance use				
Smokes cigarettes	115 (90.6%)	236 (88.7%)	351 (89.3%)	.58
Smoked or vaped marijuana[a]	69 (54.3%)	133 (50.0%)	202 (51.4%)	.42
Smoked/snorted/inhaled/vaped methamphetamine[a]	85 (66.9%)	139 (52.3%)	224 (57.0%)	.006
Smoked/snorted/inhaled crack or powder cocaine[a]	20 (15.7%)	17 (6.4%)	37 (9.4%)	.003
Smoked/snorted/inhaled/vaped either heroin or fentanyl[a]	51 (40.2%)	64 (24.1%)	115 (29.3%)	.001
Injected methamphetamine[a]	67 (52.8%)	108 (40.6%)	175 (44.5%)	.02
Injected cocaine[a]	9 (7.1%)	17 (6.4%)	26 (6.6%)	.83
Injected either heroin or fentanyl[a]	115 (90.6%)	241 (90.6%)	356 (90.6%)	.99
Mean no. of years of injection drug use (SD)	18.7 (12.2)	20.9 (11.8)	20.2 (12.0)	.06
Mean no. of times injected drugs per day[a]	2.7 (1.5)	2.4 (1.5)	2.5 (1.5)	.07
Visited shooting galleries[a]	5 (3.9%)	32 (12.0%)	37 (9.4%)	.01
Receptive needle sharing[a]	66 (52.0%)	150 (56.4%)	216 (55.0%)	.41
Crossed border to inject drugs[a]	33 (26.0%)	109 (41.0%)	142 (36.1%)	.004
Health conditions				
Tested HIV+	7 (5.6%)	26 (9.8%)	33 (8.4%)	.18
Tested HCV+	60 (47.2%)	93 (35.0%)	153 (38.9%)	.02
Has at least 1 chronic illness (excluding seasonal allergies and acne/skin problems)	57 (44.9%)	74 (27.8%)	131 (33.3%)	<.001
Mean no. of chronic conditions (excluding seasonal allergies and acne/skin problems; SD)	0.9 (1.5)	0.4 (0.8)	0.6 (1.1)	<.001
Protective behaviors during the COVID-19 pandemic				
Social distancing	41 (32.3%)	64 (24.1%)	105 (26.7%)	.09
Isolated or quarantined itself	11 (8.7%)	9 (3.4%)	20 (5.1%)	.05
Wore face mask	86 (67.7%)	206 (77.4%)	292 (74.3%)	.04
Increased handwashing/sanitizer	29 (22.8%)	20 (7.5%)	49 (12.5%)	<.001
Engaged in at least 1 protective behavior	105 (82.7%)	244 (91.7%)	349 (88.8%)	.008
Enrolled in a methadone or buprenorphine program[a]	10 (7.9)	15 (5.6)	25 (6.4)	.40
COVID-19-related disinformation (ie, endorsement of conspiracy theories)				
Thinks that the pharmaceutical industry created the COVID-19 virus	86 (67.7%)	117 (44.0%)	203 (51.7%)	<.001
Thinks that the coronavirus was created by the Chinese government as a biological weapon	91 (71.7%)	151 (56.8%)	242 (61.6%)	.005
Thinks that vaccines given to children for diseases like measles and mumps cause autism	100 (78.7%)	150 (56.4%)	250 (63.6%)	<.001

Table 1. Continued

Baseline Characteristics	Vaccine Hesitant N = 127	Not Vaccine Hesitant N = 266	Total N = 393	*P*
Thinks that COVID vaccines being offered to "people like me" are not as safe as other COVID vaccines	65 (51.2%)	95 (35.7%)	160 (40.7%)	.004
Thinks that COVID vaccines include a tracking device	66 (52.0%)	69 (25.9%)	135 (34.4%)	<.001
Thinks that some COVID vaccines could change their DNA	57 (44.9%)	64 (24.1%)	121 (30.8%)	<.001
Mean no. of conspiracies they believe (out of 6) (SD)	3.7 (1.6)	2.4 (1.9)	2.8 (1.9)	<.001
COVID-19-related misinformation (ie, incorrect knowledge items)				
Does not think that the virus that causes COVID-19 can be easily spread from 1 person to another	30 (23.6%)	54 (20.3%)	84 (21.4%)	.45
Does not think that many thousands of people have died from COVID-19	19 (15.0%)	23 (8.6%)	42 (10.7%)	.06
Thinks that most people already have immunity to COVID-19	85 (66.9%)	165 (62.0%)	250 (63.6%)	.35
Thinks that you can tell someone has COVID-19 by looking at them	48 (37.8%)	66 (24.8%)	114 (29.0%)	.008
Thinks that there are effective treatments for COVID-19 that can cure most people	96 (75.6%)	211 (79.3%)	307 (78.1%)	.40
Thinks that having COVID-19 is about as dangerous as having the flu	82 (64.6%)	169 (63.5%)	251 (63.9%)	.84
Does not think that COVID vaccines are safe for pregnant women	109 (85.8%)	141 (53.0%)	250 (63.6%)	<.001
Most important source of COVID-19-related information				
Friends[b]	59 (48.0%)	137 (52.1%)	196 (50.8%)	.45
Doctors/health professionals[b]	12 (9.8%)	9 (3.4%)	21 (5.4%)	.01
Social media[b]	26 (21.1%)	21 (8.0%)	47 (12.2%)	<.001
Additional COVID-19-related experiences				
Knows someone who died from COVID-19	45 (35.4%)	77 (28.9%)	122 (31.0%)	.19
Mean for: On a scale of 1 (low) to 10 (very), how worried are you of getting COVID-19 (or getting it again; SD)	4.0 (3.2)	5.4 (2.9)	5.0 (3.1)	<.001
Knows someone who has been vaccinated for COVID-19	80 (63.0%)	160 (60.2%)	240 (61.1%)	.59
Thinks they had COVID-19	21 (16.5%)	16 (6.0%)	37 (9.4%)	<.001
Has been tested for COVID-19 outside of our study	40 (31.5%)	38 (14.3%)	78 (19.8%)	<.001
Has been exposed to somebody with a positive COVID-19 test result	12 (9.4%)	12 (4.5%)	24 (6.1%)	.06
Had at least 1 COVID-19 symptom on day of interview	39 (30.7%)	69 (25.9%)	108 (27.5%)	.32
Tested SARS-CoV-2 seropositive[c]	48 (42.9%)	97 (39.8%)	145 (40.7%)	.58
Ever had a flu vaccine	59 (46.8%)	118 (44.9%)	177 (45.5%)	.72

Abbreviations: COVID-19, coronavirus disease 2019; HCV, hepatitis C virus; HIV, human immunodeficiency virus; PWID, people who inject drugs; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; SD, standard deviation.

[a]Past 6 months.

[b]Missing values: n = 6.

[c]Missing values: n = 33.

one third of participants were hesitant about COVID-19 vaccines, and almost all endorsed statements reflecting COVID-19 misinformation or disinformation. Although the dissemination of COVID-19 disinformation on social media has been reported as undermining vaccine uptake in the general population [3], we found that it was also independently associated with COVID-19 vaccine hesitancy in a disadvantaged population with limited access to the Internet. Our analysis also suggests specific intervention targets that provide avenues for improving vaccine trust and uptake in this socially marginalized population.

We found that COVID-19 disinformation, operationalized as endorsement of specific COVID-19 related conspiracy theories, was independently associated with vaccine hesitancy, whereas COVID-19 misinformation was not. Although research on COVID-19 vaccination hesitancy among substance using populations remain scarce, a study conducted with substance use disorder treatment patients also failed to link COVID-19 knowledge with trust in vaccines [18]. These findings imply that disinformation may be a stronger driver of COVID-19 vaccine hesitancy than misinformation among PWID.

The significant role of COVID-19 disinformation in influencing vaccine hesitancy extends a long-established foundation of medical mistrust among PWID who often avoid traditional clinical settings, preferring to receive prevention information and services in community-based settings [11]. This distrust, along with preferences for alternative sources of information, may lead some individuals to seek health advice online or through social media, where more false information may exist than factual, evidence-based information [19], and where COVID-19-related disinformation has been perpetuated [3].

Table 2. Factors Associated With SARS-CoV-2 Vaccine Hesitancy in Tijuana and San Diego

Baseline Characteristics	Univariate OR (95% CI)
Sociodemographics	
Male	1.02 (.63, 1.66)
Age[e]	0.97 (.95, 1.00)
Hispanic/Latinx/Mexican[e]	0.50 (.30, .85)
Speaks English[e]	1.57 (.99, 2.49)
Born in the USA[e]	2.69 (1.74, 4.15)
Primary residence in San Diego	1.70 (1.11, 2.60)
Highest year of school completed[d,e]	1.12 (1.04, 1.20)
Married or common law	0.94 (.56, 1.59)
Monthly income < 500 USD	1.28 (.82, 2.01)
Has a smart phone or access to a computer[e]	4.29 (2.60, 7.06)
Potential COVID-19 exposures	
Homeless[a,e]	1.77 (1.15, 2.71)
No. of hours spent on the street[a,e]	1.04 (1.01, 1.08)
Incarcerated[a]	1.05 (.48, 2.32)
No. of people in the same household[a,d,e]	1.00 (.99, 1.02)
Engaged in sex work[a]	0.76 (.40, 1.43)
Client of sex worker[a]	0.64 (.25, 1.66)
Exposed to someone diagnosed with COVID-19[e]	2.21 (.96, 5.06)
Income worse since COVID began[e]	0.54 (.35, .86)
Low or very low food security since COVID began[e]	0.51 (.30, .88)
Substance use	
Smokes cigarettes	1.22 (.60, 2.47)
Smoked or vaped marijuana[a,e]	1.19 (.78, 1.82)
Smoked/snorted/inhaled/vaped methamphetamine[a,e]	1.85 (1.19, 2.87)
Smoked/snorted/inhaled crack or powder cocaine[a,e]	2.74 (1.38, 5.43)
Smoked/snorted/inhaled/vaped heroin or fentanyl[a,e]	2.12 (1.35, 3.33)
Injected methamphetamine[a]	1.63 (1.07, 2.50)
Injected cocaine[a]	1.12 (.48, 2.58)
Injected heroin or fentanyl[a]	0.99 (.48, 2.05)
Years of injection drug use[d,e]	0.98 (.97, 1.00)
No. of times injected drugs per day[d,e]	1.12 (.97, 1.29)
Visited shooting galleries[a,e]	0.30 (.11, .79)
Receptive needle sharing[a]	0.84 (.55, 1.28)
Crossed border to inject drugs[a,e]	0.51 (.32, .81)
Health conditions	
Tested HIV+	0.54 (.23, 1.29)
Tested HCV+[e]	1.67 (1.08, 2.56)
Has at least 1 chronic condition (excluding seasonal allergies and acne/skin problems)[e]	2.11 (1.36, 3.28)
No. of chronic conditions (excluding seasonal allergies and acne/skin problems)[e]	1.49 (1.23, 1.80)
Protective behaviors during the COVID-19 pandemic	
Practiced social distancing[e]	1.50 (.94, 2.40)
Isolated or quarantined itself[e]	2.71 (1.09, 6.71)
Wore face mask[e]	0.61 (.38, .98)
Increased handwashing/sanitizer[e]	3.64 (1.97, 6.74)
Engaged in at least 1 protective behavior[e]	0.43 (.23, .81)
Enrolled in a methadone or buprenorphine program[a]	1.43 (.62, 3.28)
COVID-19-related disinformation (ie, endorsement of conspiracy theories)	
Thinks that the pharmaceutical industry created the COVID-19 virus[e]	2.67 (1.71, 4.16)
Thinks that the coronavirus was created by the Chinese government as a biological weapon[e]	1.93 (1.22, 3.04)
Thinks that vaccines given to children for diseases like measles and mumps cause autism[e]	2.86 (1.76, 4.67)
Thinks that COVID vaccines being offered to people like me are not as safe as other COVID vaccines[e]	1.89 (1.23, 2.90)
Thinks that COVID vaccines include a tracking device[e]	3.09 (1.98, 4.81)
Thinks that some COVID vaccines could change their DNA[e]	2.57 (1.64, 4.03)
No. of conspiracy items that they believe (out of 6)[e]	1.44 (1.28, 1.62)
COVID-19-related misinformation (ie, incorrect knowledge items)	
Does not think the virus that causes COVID-19 can be easily spread from 1 person to another	1.21 (.73, 2.02)
Does not think that many thousands of people have died from COVID-19[e]	1.86 (.97, 3.56)
Thinks that most people already have immunity to COVID-19	1.24 (.79, 1.93)
Thinks that you can tell someone has COVID-19 by looking at them[e]	1.84 (1.17, 2.90)
Thinks that there are effective treatments for COVID-19 that can cure most people[e]	0.81 (.49, 1.33)
Thinks that having COVID-19 is about as dangerous as having the flu	1.05 (.67, 1.63)
Does not think that COVID vaccines are safe for pregnant women[e]	5.37 (3.09, 9.34)
Most important source of COVID-19-related information	
Friends[b]	0.85 (.55, 1.30)
Doctors/health professionals[b,e]	3.05 (1.25, 7.45)
Social media[b,e]	3.09 (1.66, 5.75)
Additional COVID-19-related experiences	
Knows someone who died of COVID-19	1.35 (.86, 2.11)
On a scale of 1 (low) to 10 (very), how worried are you of getting COVID-19 (or getting it again)[e]	0.86 (.79, 0.93)
Knows someone who has been vaccinated for COVID-19	1.13 (.73, 1.74)
Thinks they had COVID-19[e]	3.10 (1.55, 6.16)
Has been tested for COVID-19 outside of our study[e]	2.76 (1.66, 4.59)
Has been exposed to somebody with a positive COVID-19 test result[e]	2.21 (.96, 5.06)
Had at least 1 COVID-19 symptom day of interview	1.27 (.79, 2.02)
Tested SARS-CoV-2 seropositive[c]	1.14 (.72, 1.79)
Ever had a flu vaccine	1.08 (.71, 1.66)

Abbreviations: CI, confidence interval; COVID-19, coronavirus disease 2019; HCV, hepatitis C virus; HIV, human immunodeficiency virus; OR, odds ratio; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

[a]Past 6 months.

[b]Missing values: n = 6.

[c]Missing values: n = 33.

[d]Per 1 unit increase.

[e]*P* value < .10.

Table 3. Factors Independently Associated With COVID-19 Vaccine Hesitancy Among People Who Inject Drugs in San Diego, California, USA, and Tijuana, Mexico

Baseline Characteristics	Adjusted OR[a] (95% CI)
Age[c]	0.97 (.95, 1.00)
Has low/very low food security	0.44 (.23, .87)
Has a smart phone or access to a computer	3.75 (2.07, 6.82)
Number of self-reported chronic conditions (excluding allergies and acne/other skin conditions)[c]	1.46 (1.17, 1.82)
Number of conspiracies they believe (out of 6)[c]	1.51 (1.31, 1.74)
Most important source of COVID-19 information: social media[b]	1.86 (.93, 3.70)
On a scale of 1 to 10, how worried are you of getting COVID-19 (or getting it again)[c]	0.85 (.77, .93)

Abbreviations: CI, confidence interval; COVID-19, coronavirus disease 2019; OR, odds ratio.

[a]Variables in the multivariable model were adjusted for all the variables in the model as well as for time.

[b]Missing value: n = 6;

[c]Per 1 unit increase.

Having access to smart phones or computers was strongly associated with COVID-19 vaccine hesitancy in our sample. PWID in other community-based studies increasingly report having regular access to mobile phones and the Internet, particularly within public spaces [12, 20, 21]. Although only 22% had access to either in our study, it is possible that these individuals had more resources and were influencers in their communities, sharing COVID disinformation within their networks. Citing social media as one's most important source of COVID-19 information was marginally associated with vaccine hesitancy, even after controlling for phone/computer access. When we repeated our analysis to include participants who had received at least one COVID-19 vaccine dose by 10 September 2021, the association between citing social media as one's most important source of COVID-19 information and vaccine hesitancy was even stronger.

Concerns about vaccine safety were also apparent in our sample, confirming previous research among the general population [22] and those receiving substance abuse treatment [18], which reported concerns that COVID-19 vaccines are unsafe and have been tested insufficiently [23]. These findings suggest that interventions to promote COVID-19 vaccine uptake will need to address safety concerns [24]. At the same time, the majority of our sample engaged in at least one protective measure during the COVID-19 pandemic, suggesting that many individuals already consider the severity of COVID-19, suggesting that perceived threat could be leveraged as an intervention target for this population.

Increasing confidence in vaccine safety and efficacy may be particularly important for subgroups of PWID with higher levels of skepticism or susceptibility to confirmation bias (ie, the tendency to believe information that aligns with one's existing beliefs or experiences) [25]. As others have argued [26], interventions may be more acceptable to PWID if they are delivered by trusted sources of health information and support, such as harm reduction outreach workers, street medicine providers, recovery coaches, peers, or staff of other community-based organizations that are frequented and trusted by this population, like shelters, community centers, hostels, libraries, and other public spaces.

Interestingly, we found no evidence to support our hypothesis that Latinx participants were more likely to be vaccine hesitant, as others have reported [2, 7]. In fact, our unadjusted analysis found that PWID who were White and those born or living in San Diego were more likely to be vaccine hesitant than those who were Latinx or born or living in Mexico. Contrary to general population-based samples in the United States [27], we did not find educational attainment to be independently associated with vaccine hesitancy.

PWID reporting food insecurity and those with higher levels of concern about SARS-CoV-2 were less hesitant about COVID-19 vaccines. However, two thirds of our sample reported willingness to get vaccinated, but only 7.6% had received at least 1 dose by 10 September 2021, highlighting the urgent need to increase uptake. Of concern, participants who had a greater number of comorbidities such as diabetes and hypertension were more vaccine hesitant than others. This is worrisome because these individuals could be more vulnerable to severe COVID-19 complications and would most benefit from protection. Furthermore, a recent study found that compared to other patients, people with substance use disorders were more likely to experience breakthrough infections following COVID-19 vaccination, which was partly attributed to their high prevalence of comorbid conditions [9].

Our findings suggest that structural supports including financial incentives for vaccination that have been successful with other vulnerable populations could also be beneficial for PWID [28]. These include transportation assistance, co-location with other routinely accessed services (eg, syringe exchanges, food banks, soup kitchens), concurrent vaccination of peers and family members, and vaccine administration by an expanded group of healthcare and lay providers (eg, emergency department and drug treatment clinic personnel, community health workers). Modest financial incentives via conditional cash transfers and contingency management have demonstrated success in increasing adherence to 3-dose hepatitis B vaccines among PWID and other substance using populations [29, 30].

Limitations of this study include the cross-sectional nature of the analysis, which precludes our ability to determine causal associations. Although this was a binational study, sampling was nonrandom, and results may not generalize to other samples of PWID. We also relied on self-report and recall for many behaviors, which may have been subject to socially desirable responding. Although the COVID-19 disinformation scale we utilized had good internal consistency, other COVID-19 related knowledge measures have only been recently developed and, to our knowledge, have not been validated in this or other populations impacted by substance use. Our analysis excluded participants who were recruited before

survey items on COVID-19 knowledge and vaccine hesitancy were developed. Since attitudes to COVID-19 vaccines may have changed over time, we controlled for time in our analysis. Future longitudinal, qualitative, and intervention-development studies are needed to better understand contextual factors influencing vaccine hesitancy in this population to identify strategies to best address these intervention targets.

In conclusion, we identified a concerning level of COVID-19 vaccine hesitancy among community-recruited PWID in the San Diego-Tijuana border region, which was associated with COVID-19 related disinformation, reliance on social media as a source health information, younger age and comorbidities. Interventions that increase accurate COVID-19 vaccine knowledge, trust, and motivation, while also reducing structural barriers to COVID-19 vaccine access are urgently needed to reduce morbidity and mortality in this vulnerable population.

Notes

Author contributions. S. A. S. designed the study and most survey instruments, conceived of the research questions wrote and edited the manuscript. D. A. conducted the data analysis, prepared the results, and edited the manuscript. G. R. helped design the study, oversaw data collection in Tijuana, and edited the manuscript. A. H. V. designed and pre-tested the survey, oversaw collection of laboratory specimens, and edited the manuscript. C. V. oversaw and participated in data collection in San Diego and edited the manuscript. I. A. programmed the study instrument, oversaw data management, and edited the manuscript. T. P. helped design the study and survey instruments and edited the manuscript. R. A. M. assisted with the literature review and edited the manuscript. A. R. B. helped interpret the analysis and wrote and edited the manuscript.

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Data sharing. De-identified data used in this analysis are available after completion of the study in May 2022. Interested parties should contact Daniela Abramovitz at dabramovitz@health.ucsd.edu for more information on how to submit a data request.

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