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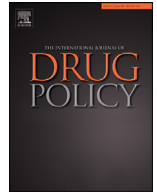
Research Paper

Mortality by cause of death during year 1 of the COVID-19 pandemic in a cohort of older adults from Baltimore Maryland who have injected drugs[☆]

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ARTICLE INFO

ABSTRACT

Background: In 2020, the first year of the COVID-19 pandemic, overdose deaths increased. However, no studies have characterized changes in mortality during the pandemic in a well-characterized cohort of people who use drugs in active follow-up at the time of pandemic onset.

Design: We compared all-cause and cause-specific mortality in the first year of the pandemic (Mar–Dec 2020) to the five years preceding (Jan 2015–Feb 2020), among participants in the AIDS Linked to the IntraVenous Experience (ALIVE) study: a community-recruited cohort of adults from Baltimore who have injected drugs. 3510 participants contributed 17,498 person-years [py] of follow-up time. Cause and dates of death were ascertained through the National Death Index. Comparisons were made for the full cohort and within subgroups with potentially differential levels of vulnerability.

Results: All-cause mortality in 2020 was 39.6 per 1000 py, as compared to 37.2 per 1000 py pre- pandemic (Adjusted Incidence Rate Ratio = 1.09, 95%: confidence interval: 0.84–1.41). Increases were mostly attributable to chronic disease deaths; injury/poisoning deaths did not increase. No pre-post differences were statistically significant.

Conclusion: In this exploratory analysis of an older cohort of urban-dwelling adults who have injected drugs, mortality changes during the first year of the pandemic differed from national trends and varied across potentially vulnerable subgroups. More research is needed to understand determinants of increased risk of mortality during the pandemic among subgroups of people who use drugs.

Background

In the first years of the COVID-19 pandemic, all-cause mortality increased globally and in most countries around the world (Ahmad et al., 2021; Islam et al., 2021; Wang et al., 2022). The majority of this increase was likely attributable to deaths caused by COVID-19, although many are not properly diagnosed as such (Wang et al., 2022; Wu et al., 2021). However, there is evidence other causes of death also increased, including chronic disease deaths (Wu et al., 2021).

Of particular importance to the health of people who use drugs are large increases in drug overdose deaths in the first years of the pandemic, principally in United States (National Center for Health Statistics, 2022a) and Canada (Health Canada, 2020). The cause of this increase in overdose deaths in North America is not fully understood. Several hypotheses have been posited to explain the surge in overdose deaths during the COVID-19 pandemic (Cantor et al., 2021; Czeisler, 2020; Friedman et al., 2021; Galarneau et al., 2021; Gleason et al., 2022; Holingue et al., 2020; Russell et al., 2021; Wakeman et al., 2020). Data from multiple states suggest that much of the increase in overdose deaths was attributable to an increase in deaths involving fentanyl (Currie et al., 2021; Macmadu et al., 2021; Maryland Department of Health, 2021), suggesting pandemic-related disruptions to the drug market may have made the drug supply in North America more dangerous. There is also evidence that the increase in overdose deaths was larger than the increase in overdose incidents, suggesting

each overdose event was more likely to result in death (Friedman et al., 2021).

However, understanding how the COVID-19 pandemic has impacted mortality among people who use drugs requires more than simply examining trends in overdose deaths. As compared to the general population, people who use illicit drugs are more likely to have immunocompromising conditions such as HIV that could increase risk for severe COVID-19 (Handanagic, 2021; Sun et al., 2021); more likely to be exposed to COVID-19 in correctional settings, which have elevated COVID-19 mortality (Saloner et al., 2020); and more likely to die from chronic diseases (Sun et al., 2021), for which care may have been disrupted during the pandemic (Chudasama et al., 2020; Hacker, 2021).

This report compares estimates of all-cause, injury-and-poisoning-related, and other sources of mortality before and after the start of the COVID-19 pandemic – defined here as March 1, 2020 – in a community-based cohort of adults who have a history of injecting drugs. Trends in all-cause and cause-specific mortality over a 30-year period in this cohort were previously described (Genberg et al., 2021; Sun et al., 2021), and we observed increasing trends in overdose and drug-related deaths up to 2018. By examining a cohort of adults under observation before the start of the pandemic, we can better understand the pandemic' effect on multiple causes of mortality in people who inject drugs (as opposed to just drug overdose death). Further, by leveraging previously collected health data, we can examine if pandemic-associated changes in mortality differed across health-related sub-populations of people who have injected drugs.

Methods

Participants

Study participants were enrolled in the AIDS Linked to the Intra-Venous Experience (ALIVE) study. ALIVE is a community-recruited cohort of adults (18 years or older at enrollment) who have injected drugs and live in or near Baltimore, Maryland. Enrollment began in 1988, with additional recruitment occurring in 1994–1995, 1998, 2000, 2005–2008, and 2015–2018. Details of ALIVE's methods are described elsewhere (Vlahov et al., 1991). Briefly, participants attend twice-annual follow-up visits where they complete a standardized questionnaire (part interviewer-administered, part audio-computer-assisted self-administered) on substance use behaviors, comorbidities, and social and behavioral disease risk, provide blood samples for infectious disease testing, and complete a brief clinical examination. Participants remained enrolled in ALIVE until such time as they ask to withdraw from the study or die. Participants provide informed consent for all study activities, including annual identity matches with the National Death Index in order to capture dates and causes of. Importantly, this means that ascertainment of death is complete for all participants ever enrolled in ALIVE – even those who stop attending study visits for very long periods of time – so long as participants do not proactively inform ALIVE they are withdrawing from the study. The Johns Hopkins University institutional review board approved the study and all participants provided informed written consent.

There were 3522 study participants alive on January 1, 2015. Of these, 3510 (>99%) had complete data on time-fixed covariates from their baseline study visit (see 2.2 "Measures") and were included in the *primary analysis cohort*; these 3510 participants contributed 17,498 (>99%) person-years of follow-up time.

A smaller, *secondary subsample* was also analyzed, where we imposed the additional criteria that participants must have attended at least one study visit since January 1, 2014, and at least one of those visits provided data on each drug use, social, and health-related covariate used in the secondary analysis (see 2.2 "Measures"). This secondary analysis was conducted to analyze additional time-varying covariates that are assessed at study visits. This secondary cohort includes 1630 participants (46%) contributing 7378 person-years (42%).

Measures

Dates and underlying causes of death through December 31, 2020 were identified through linkage to the National Death Index 2015–2020 final release (Centers for Disease Control & Prevention, 2021). Causes of death were categorized based on ICD-10 codes into five groups: 1) COVID-19 (ICD Code U07.1), 2) injury or poisoning deaths, 3) chronic disease deaths, 4) infectious disease deaths other than COVID-19, and 5) all other causes of death that occurred in this cohort. Details of ascertainment and classification have been previously described (Sun et al., 2021). ICD-10 codes present in this sample corresponding to each cause of death category are shown in Appendix Table 4. Ascertainment of death was complete for all enrolled participants, regardless of whether they had a follow-up visit during the study period.

Time-fixed covariates assessed at baseline were included in the analysis of the *primary cohort*: age on January 1, 2015 (18–49, 50–59, 60 or older), self-reported gender at baseline (male, female); education (less than high school, high school or higher); and whether participants were late entries into the study cohort (recruited before January 1, 2015; recruited after January 1, 2015).

Additionally, time-varying covariates assessed at bi-annual study visits since 2014 were included in the analysis of the *secondary subsample*: a four-level categorical variable for any drug use in the six months before the visit (any injection drug use, use of any illicit drugs other than marijuana that were not injected, marijuana use only, no illicit drug use); any cigarette use in the past six months; any alcohol use in the past six months; depressive symptoms, defined as a score of 23 or higher on the Center for Epidemiologic Studies Depression Scale (CESD) (Eaton et al., 2004); reported being employed at the time of the study visit; experienced homelessness in the past six months; hepatitis C virus (HCV) antibody positive; HIV antibody positive; obesity, defined as BMI >= 30; and a count (0, 1, 2, 3 or more) of self-reported history of comorbid health conditions (including diabetes, high cholesterol, high blood pressure, stroke, renal disease, and lung disease).

Analytic approach

As noted above, we conducted: 1) An analysis of the *primary cohort* with the full sample, to maximize sample size and representativeness of the population of people who inject drugs in Baltimore. 2) An analysis of the *secondary subsample* of participants who attended at least one study visit, to examine more potentially interesting subgroups that may vary in their vulnerability to mortality. Other than the sample size and covariates analyzed, the approach was identical.

Additionally, the approach was the same for all-cause and each specific cause of mortality, except that in each cause-specific analysis, deaths from causes other than the cause of interest in that analysis were not counted, and participants were censored following their competing-cause of death.

All participants, except those who were enrolled after January 1, 2015 ("late entries"), began contributing person time on January 1, 2015. Late entries began contributing person time on the date of their first study visit. Participants' time-fixed covariate values were drawn from their baseline study visit. Participants' initial time-varying covariates were drawn from their last study visit in 2014, or (for late entries) their first study visit and updated at each study visit. Because participants did not attend regular study visits during the pandemic, no covariate updates were conducted after March 1, 2020. Participants continued to contribute person time until they died, or until they were administratively censored on December 31, 2020.

Mortality rates per 1000 person years were estimated for the pre-pandemic (January 1, 2015-February 29, 2020) and pandemic (March 1, 2020–December 31, 2020) periods respectively by dividing the number of deaths by the number of person-years at risk during that period and multiplying by 1000. Mortality during the pandemic was then compared

to mortality prior to the pandemic using crude and adjusted (see below) rate ratios.

To account for potential confounding or survival bias induced by changes in the observed characteristics (see 2.2. Measures) of the cohort (Amoah et al., 2020), we repeated the analysis using propensity score weighting (Amoah et al., 2020). This was done because, if we simply observe crude mortality differences between pandemic and pre-pandemic periods, these differences might be partly or entirely due to changes in the characteristics of the cohort over time. For example, some participants who were previously not using illicit drugs might resume use right before the onset of the pandemic, putting the cohort incidentally at higher risk for death during the pandemic (i.e. "confounding bias"). Or, for example, older or male participants may be less likely to survive to the start of the pandemic, leaving the pandemic cohort at lower risk for death (i.e. "survival bias"). Specifically, for adjusted rate ratios, we estimated a propensity score indicating the probability of each person period occurring during pandemic conditional on all time-fixed and (in the secondary subsample for which they were available) time-varying covariates. Propensity scores were estimated using logistic regression. Person periods not in the pandemic were then weighted by the predicted odds those intervals occurred during the pandemic (i.e. "average treatment effect on treated" weights), and the relative rate was re-estimated in this weighted sample (Sato & Matsuyama, 2003). Standardized mean differences in study covariates before and after weighting are shown in Appendix Table 5, to verify weighting improved covariate balance.

Within each subgroup defined by covariates used in the analysis (e.g., participants' age 18–49, male participants, participants who injected drugs, etc.) incidence rates and relative rates were estimated using the same methods described above, but for members of that subgroup alone. These subgroup analyses were conducted for all-cause and injury/poisoning mortality.

For all incidence rate ratios, we estimate 95% Wald confidence intervals. Because the number of deaths during the pandemic was likely too small to detect interaction effects using hypothesis testing, potentially scientifically meaningful between-subgroup differences in our estimate of the association of the pandemic with mortality are noted in the text.

Finally, historically, the ALIVE cohort has had much higher mortality than Baltimore City (Sun et al., 2021). To provide context, we conducted a supplemental analysis comparing mortality in this study cohort to Baltimore City. Specifically, for 2019 and 2020 respectively, we computed age-by-sex-stratified mortality rates for this study cohort, standardized to the Baltimore City population age 15–85, and compared these standardized mortality estimates to publicly available mortality estimates for Baltimore for that same age group using a standardized mortality ratio (Maryland Department of Health, 2021).

All analyses were conducted in R Version 3.4.3 (R Core Team, 2017).

The manuscript was not pre-registered, and all results should be considered exploratory.

Results

Description of sample

In the primary analytic sample, in the pre-pandemic period, 44.3% of person-years were contributed by persons over 50 years of age and 67.7% by persons over 60; 71.9% were contributed by male participants; 76.9% by Black participants; and 53.7% by participants who did not complete high school. Participants alive during the pandemic were demographically similar to participants alive before the pandemic. Detailed pre- and intra-pandemic demographics for primary and secondary samples are shown in Table 1. Person-level demographics are shown in Appendix Table 1.

Changes in mortality in the "Primary" cohort containing the full sample

During the pandemic, 96 participants in the primary cohort died, corresponding to an all-cause mortality rate (MR) of 39.6 per 1000 person years [py]; this was 7% higher than the period before the pandemic (37.2 per 1000 py), but this difference was not statistically significant (incidence rate ratio [IRR] of 1.07, 95% confidence interval [CI] 0.86–1.32). This difference did not change appreciably after adjustment (adjusted IRR: 1.09; 95% CI 0.84–1.41) (Table 2). There were no statistically significant changes in injury/poisoning mortality (pre-pandemic 13.2 per 1000 py, pandemic 13.6 per 1000 py; IRR 1.03, 95% CI 0.71 to 1.49; adjusted IRR [aIRR] 0.95, 95% CI 0.62 to 1.47) (Table 3); chronic disease mortality (pre-pandemic 17.0 per 1000 py, pandemic 18.1 per 1000 py; IRR 1.07, 95% CI 0.78 to 1.47; aIRR 1.14, 95% CI 0.77 – 1.67) (not shown in tables); or infectious disease mortality (excluding COVID-19) deaths (pre-pandemic 5.0 per 1000 py, post-pandemic 4.1 per 1000 py; IRR 0.82, 95% CI 0.42 to 1.58; aIRR 0.93, 95% CI 0.43 to 2.03) (not shown in tables). Results were similar in all subgroup specific analyses. Four of the observed deaths were due to COVID-19 (MR: 1.65 per 1000 person-years).

Changes in mortality in the "Secondary" subsample of participants with at least one study visit

Results were qualitatively similar and non-significant in the secondary cohort of participants who attended at least one study visit. As in the primary cohort, all subgroup analyses were also non-significant (Appendix Tables 2 and 3); however, one notable difference in pre-post mortality was that all-cause mortality increased among persons who were HCV antibody negative (IRR 2.14, 95% CI 1.09 to 4.12; aIRR 2.03, 95% CI 0.74 to 5.61); but decreased among those who were HCV antibody positive (IRR 0.94, 95% CI 0.66 to 1.34; aIRR 0.96, 95% CI 0.59 to 1.55).

Supplemental analysis: comparison to Baltimore city

In supplemental analysis, after standardizing to the age and sex distribution of the Baltimore City population age 15 to 85, the all-cause mortality rate in this study cohort in 2019 was 2907 deaths per 100,000, as compared to a rate of 1099 per 100,000 for Baltimore City in the same year (standardized mortality ratio [SMR] 2.65). In 2020, again standardized to Baltimore's age and sex distribution, this cohort's mortality rate was 2795 per 100,000, as compared to 1303 per 100,000 for Baltimore (SMR 2.15).

Discussion

In this cohort of older, mostly Black adults from the Baltimore area with a history of drug use, all-cause mortality increased by 7% during the first 9 months of the COVID-19 pandemic in the US as compared to the five years prior. This increase was not statistically significantly different than 0%. However, it is important to note that the confidence interval for the overall mortality increase (−14% to 32%) also included the estimated increases in mortality for the US general population (15%) and Baltimore (19%) from 2019 to 2020 respectively (National Center for Health Statistics, 2022b). Thus, we think the best interpretation of the mortality increase observed in this cohort is that its magnitude is generally consistent with the increase that we know occurred in the general population over a similar time period.

The observed increase in mortality in this cohort was primarily driven by increases in deaths due to chronic disease; this increase in chronic disease mortality is a continuation of what was observed pre-pandemic (Sun et al., 2021). Additionally, four cohort participants died of COVID-19. Injury and poisoning deaths – of which 71% in this sample were drug or alcohol-related poisoning and another 17% were poison-

Table 1

Demographic, social, drug use, and health-related characteristics of a cohort of older adults (*n* = 3510) who have injected drugs before and during the COVID-19 pandemic—Maryland, 2015–2020.

| Demographic | All cohort participants alive as of Jan 1, 2015 | | | | Cohort participants with a study visit since Jan 1, 2014 | | | |
| | Pre-Pandemic | | Pandemic | | Pre-Pandemic | | Pandemic | |
	Total Person Years	Percent of Person Years	Total Person Years	Percent of Person Years	Total Person Years	Percent of Person Years	Total Person Years	Percent of Person Years
All	15,073	100.0%	2426	100.0%	6239	100.0%	1140	100.0%
Age Group								
18–49	4872	32.3%	901	37.2%	2349	37.7%	520	45.6%
50–59	6671	44.3%	1029	42.4%	2816	45.1%	458	40.2%
60+	3530	23.4%	495	20.4%	1073	17.2%	162	14.2%
Gender								
Male	10,841	71.9%	1736	71.6%	4227	67.8%	776	68.1%
Female	4231	28.1%	689	28.4%	2012	32.2%	364	31.9%
Race								
Not Black	3482	23.1%	620	25.6%	1251	20.1%	290	25.5%
Black	11,590	76.9%	1805	74.4%	4988	79.9%	850	74.5%
Education								
Less than high school	8094	53.7%	1287	53.0%	3347	53.7%	591	51.8%
High school or more	6978	46.3%	1139	47.0%	2891	46.3%	549	48.2%
Recruitment Cohort								
All other recruitment waves	12,444	82.6%	1815	74.8%	4478	71.8%	665	58.4%
2015–2018	2628	17.4%	611	25.2%	1760	28.2%	475	41.6%
Any Illicit Drug Use[a]								
No illicit drug use	–	–	–	–	2739	43.9%	456	40.0%
Marijuana only	–	–	–	–	262	4.2%	58	5.1%
Illicit drugs, no injecting	–	–	–	–	1105	17.7%	229	20.1%
Injected drugs	–	–	–	–	2132	34.2%	396	34.8%
Any cigarettes								
No	–	–	–	–	1368	21.9%	238	20.9%
Yes	–	–	–	–	4871	78.1%	902	79.1%
Any alcohol								
No	–	–	–	–	3200	51.3%	596	52.3%
Yes	–	–	–	–	3039	48.7%	544	47.7%
Elevated depressive symptoms								
No	–	–	–	–	4448	71.3%	806	70.7%
Yes	–	–	–	–	1791	28.7%	334	29.3%
Employed								
No	–	–	–	–	5260	84.3%	965	84.7%
Yes	–	–	–	–	979	15.7%	175	15.3%
Homeless								
No	–	–	–	–	5367	86.0%	951	83.4%
Yes	–	–	–	–	872	14.0%	189	16.6%
HCV Ab+	–	–	–	–				
No	–	–	–	–	1320	21.2%	264	23.2%
Yes	–	–	–	–	4918	78.8%	876	76.8%
HIV Ab+								
No	–	–	–	–	4466	71.6%	832	73.0%
Yes	–	–	–	–	1773	28.4%	308	27.0%
Obese								
No	–	–	–	–	4400	70.5%	798	70.0%
Yes	–	–	–	–	1838	29.5%	343	30.0%
Number of chronic comorbidities								
0	–	–	–	–	2156	34.6%	401	35.2%
1	–	–	–	–	1943	31.1%	343	30.1%
2	–	–	–	–	1175	18.8%	216	18.9%
3+	–	–	–	–	965	15.5%	179	15.7%

[1] The start of the COVID-19 pandemic was defined as March 1, 2020.

[2] All time varying covariates assessed in six months preceding the study visit.

[a] Variables including and below "Any Illicit Drug Use" are measured at biannual study visits, and are therefore only available in the secondary subsample of participants who have attended at least one visit since 2015.

Table 2

Comparison of all-cause mortality rates during the COVID-19 pandemic vs before in a cohort of adults (*n* = 3510) who have injected drugs – all study participants.

Subgroup	Died Pre-Pandemic		Died During Pandemic		Incidence Rate Ratio, Pre- vs During Pandemic	
	Count	per 1000 person-years	Count	per 1000 person-years	Crude	Adjusted
All	560	37.2	96	39.6	1.07 (0.86–1.32)	1.09 (0.84–1.41)
Age Group						
18–49	125	25.7	24	26.6	1.04 (0.67–1.61)	1.01 (0.61–1.69)
50–59	244	36.6	48	46.6	1.28 (0.94–1.74)	1.27 (0.87–1.87)
60+	191	54.1	24	48.5	0.90 (0.59–1.37)	0.92 (0.57–1.50)
Gender						
Male	406	37.4	66	38.0	1.02 (0.78–1.32)	1.02 (0.75–1.39)
Female	154	36.4	30	43.5	1.20 (0.81–1.77)	1.24 (0.76–2.02)
Race						
Not Black	110	31.6	26	41.9	1.33 (0.87–2.03)	1.31 (0.80–2.13)
Black	450	38.8	70	38.8	1.00 (0.78–1.28)	1.00 (0.73–1.35)
Education						
Less than high school	304	37.6	55	42.7	1.14 (0.85–1.52)	1.16 (0.82–1.64)
High school or more	256	36.7	41	36.0	0.98 (0.71–1.36)	0.99 (0.67–1.46)
Recruitment Cohort						
All other recruitment waves	468	37.6	79	43.5	1.16 (0.91–1.47)	1.17 (0.88–1.56)
2015–2018	92	35.0	17	27.8	0.80 (0.47–1.33)	0.81 (0.44–1.49)

[1] Adjusted analysis adjusted for age, gender, race, education, cohort using propensity score weighting (see Analytic Approach).

Table 3

Comparison of injury and poisoning mortality rates during the COVID-19 pandemic vs before in a cohort of adults (*n* = 3510) who have injected drugs – all study participants.

	Died Pre-Pandemic		Died During Pandemic		Incidence Rate Ratio, Pre- vs During Pandemic	
	Count	per 1000 person-years	Count	per 1000 person-years	Crude	Adjusted
All	199	13.2028	33	13.6052	1.03 (0.71–1.49)	0.95 (0.62–1.47)
Age Group						
18–49	90	18.4743	16	17.7484	0.96 (0.56–1.64)	0.88 (0.48–1.63)
50–59	79	11.8418	15	14.5775	1.23 (0.71–2.14)	1.23 (0.62–2.44)
60+	30	8.49946	2	4.0398	0.48 (0.11–1.99)	0.48 (0.10–2.26)
Gender						
Male	157	14.4814	29	16.7041	1.15 (0.78–1.71)	1.07 (0.67–1.71)
Female	42	9.92662	4	5.80172	0.58 (0.21–1.63)	0.57 (0.18–1.83)
Race						
Not Black	66	18.9532	12	19.3489	1.02 (0.55–1.89)	1.04 (0.52–2.08)
Black	133	11.4751	21	11.632	1.01 (0.64–1.61)	1.00 (0.57–1.76)
Education						
Less than high chool	97	11.9835	19	14.7664	1.23 (0.75–2.01)	1.15 (0.64–2.08)
High school or more	102	14.6172	14	12.2932	0.84 (0.48–1.47)	0.78 (0.41–1.48)
Recruitment Cohort						
All other recruitment waves	138	11.0894	22	12.1234	1.09 (0.70–1.71)	1.07 (0.63–1.83)
2015–2018	61	23.2095	11	18.007	0.78 (0.41 - 1.47)	0.74 (0.35–1.55)

[1] Adjusted analysis adjusted for age, gender, race, education, cohort.

ings without a causal substance identified – did not increase appreciably in this cohort during the early COVID-19 pandemic.

While, as noted above, the magnitude of increase in all-cause mortality observed in this cohort was comparable to increases observed locally and nationally, we did not observe a larger increase in injury and poisoning deaths specifically, despite drug overdose deaths increasing nationally, in Maryland, and in Baltimore City (Maryland Department of Health, 2021; Products - Vital Statistics Rapid Release - Provisional Drug Overdose Data, 2021). However, it is important to note that injury and poisoning mortality in this cohort nearly doubled over the past decade, and overall mortality in this cohort was much higher than the general population of Baltimore before the pandemic, and remained so during the pandemic. It is difficult to predict how much increase in mortality from any cause would have been expected in this cohort by an exogenous shock like the COVID-19 pandemic.

It is also possible that characteristics of this cohort shielded some members from pandemic-associated increases in mortality. In particular, prior research is consistent with the hypothesis that increasing potency of the drug supply due to fentanyl contamination was a major driver of mortality (Cantor et al., 2021; Czeisler, 2020; Friedman et al.,

2021; Galarneau et al., 2021; Gleason et al., 2022; Holingue et al., 2020; Russell et al., 2021; Wakeman et al., 2020). It is possible that members of this cohort of older adults who survived to the start of the pandemic – particularly members who may have used drugs more frequently or heavily in the past – may have strategies that helped them avoid drug-related death increases during the pandemic. Notably, within this cohort, injury/poisoning mortality declined among persons with a history of HCV infection, but increased among those without HCV infection, although this difference was not statistically significant. Past research shows HCV infection could be a proxy marker for more frequent drug use over the life course (Hahn et al., 2002; Villano et al., 1997), so this is consistent with the hypothesis that people with heavier drug use over the life course who managed to survive up to the start of the pandemic were more able to navigate the risks of the pandemic, for example because they may be more engaged with health or harm reduction services. Other studies suggest people who survive overdoses adopt risk-reduction strategies that they believe have helped them prevent repeat overdoses (Elliott et al., 2019; Mistler et al., 2021). However, the data here are insufficient to strongly support any particular hypothesis about why this cohort did not experience increases in drug overdose mortality

as observed in the broader U.S., Maryland, and Baltimore populations. Additional research is necessary to understand overdose during the pandemic among aging populations of people who use drugs.

Limitations

First, as discussed, this is a cohort of older, predominantly Black adults from the Baltimore area and is thus not representative of all people who use drugs in the United States. Second, because of limitations on data collection during the pandemic, we could not examine the impact of behavior changes during the pandemic (if any) on mortality trends. This is a focus of ongoing, qualitative research. Third, while we adjusted for several potential confounders, members of this cohort who survived to the start of the pandemic may differ in unmeasured ways from cohort members who died in the years leading up to the pandemic. These unmeasured qualities of "survivors" could contribute to the lack of increased mortality from injury and poisoning during the pandemic. Finally, only mortality from the first nine months of the pandemic were available and included in this analysis. Future investigations will examine the longer-term impacts of the COVID-19 pandemic on mortality, particularly in chronic disease and other causes that may have been influenced by delayed care-seeking during the pandemic.

Conclusion

In the first months of the COVID-19 pandemic, we observed a modest non-statistically significant increase in mortality in this Baltimore-area cohort of older adults who have a history of injecting drugs that was roughly consistent in magnitude with increases in mortality observed in the surrounding community. The non-significant increase we observed was attributable to chronic disease deaths and COVID-19 deaths. Baseline mortality in this cohort was very high relative to the general population before the pandemic, so it is difficult to know how much more mortality could have increased. We have also speculated here that some older people who have used drugs may have developed strategies that also helped them avoid increases in fatal overdose during the COVID-19 pandemic, although this exceeds the scope of what can be known from the data here. Finally, there were also an enormous diversity of complex public health and social measures enacted and lifted at various points during the early months of the pandemic including stay at home orders, closure of public spaces, and mask mandates. Research shows many of these strategies helped prevent COVID-19 infections and deaths (Carroll & Prentice, 2021; Fowler et al., 2021; Jiang et al., 2019; Medline et al., 2020; Yilmazkuday, 2021), but they also disrupted essential services for people who use drugs (Feder et al., 2022). Our study cannot elucidate any unique impacts these policies may have had on people who use drugs as compared to the general population. However, elucidating the impact of these policies – as well as strategies, behaviors, or characteristics that may have helped prevent increases in drug-related mortality in

this cohort – may inform strategies for preventing harm to other adults who use drugs, and are important areas for future research.

Because of the descriptive nature of this study, its policy and practice implications of this study are limited. However, we think this study does underscore two points relevant policymakers and practitioners seeking to protect the health of people who use drugs. The first is that it reiterates the disproportionate burden of chronic disease in the life of people who have used drugs, and the importance of investing in strategies that help link people who use drugs to basic health care necessary for disease management such as integration of addiction medicine into primary medical care (Wakeman & Barnett, 2018). Second, the somewhat surprising findings here are a reminder that administrative statistics tracking overdose deaths paint an incomplete picture of the health of people who use drugs, since overdose trends may reflect trends that exist only or mostly among certain sub-populations of people who use drugs. Drug policy needs to also be informed by rigorous collection of data and information from people who use or have used illicit drugs – to understand the range of health challenges and protective factors that exist in this population – as a supplement to focusing on administrative indicators of the health outcomes most directly linked to drug use like overdose.

Ethics approval

The authors declare that they have obtained ethics approval from an appropriately constituted ethics committee/institutional review board where the research entailed animal or human participation.

Johns Hopkins Bloomberg School of Public Health

Declarations of interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Funding

Appendix

See Tables A1, A2, A3, A4, A5

Table A1

Characteristics of a cohort of older adults who have injected drugs before and during the COVID-19 pandemic—Maryland, 2015–2020.

Demographic	Pre-Pandemic		Pandemic[a]	
	Total Participants	Percent of Participants	Total Participants	Percent of Participants
All Participants	3510	100%	2950	100%
Age Group				
18–49	1216	35%	1091	37%
50–59	1498	43%	1254	43%
60+	796	23%	605	21%
Gender				
Male	2517	72%	2111	72%
Female	993	28%	839	28%
Race				
Not Black	865	25%	755	26%
Black	2645	75%	2195	74%
Education				
Less than high chool	1870	53%	1566	53%
High school or more	1640	47%	1384	47%
Recruitment Cohort				
All other recruitment waves	2681	76%	2213	75%
2015–2018	829	24%	737	25%
With Time-Varying Covariates[b]	1630	100%	1387	100%
Any illicit drug Use				
No illicit drug use	599	37%	554	40%
Marijuana only	50	3%	71	5%
Illicit drugs, no injecting	227	14%	282	20%
Injected drugs	754	46%	480	35%
Any cigarettes				
No	276	17%	289	21%
Yes	1354	83%	1098	79%
Any alcohol				
No	743	46%	724	52%
Yes	887	54%	663	48%
Elevated depressive symptoms				
No	1125	69%	979	71%
Yes	505	31%	408	29%
Employed				
No	1412	87%	1176	85%
Yes	218	13%	211	15%
Homeless				
No	1316	81%	1156	83%
Yes	314	19%	231	17%
HCV Ab+				
No	357	22%	322	23%
Yes	1273	78%	1065	77%
HIV Ab+				
No	1175	72%	1014	73%
Yes	455	28%	373	27%
Obese				
No	1165	71%	970	70%
Yes	465	29%	417	30%
Number of chronic comorbidities				
0	618	38%	486	35%
1	501	31%	420	30%
2	304	19%	262	19%
3+	207	13%	219	16%

[a] The sample size during the pandemic is smaller than pre-pandemic because some participants died before the start of the pandemic.

[b] Pre-pandemic time-varying covariates come from the participant's first pre-pandemic visit. Pandemic time-varying covariates come from participants first pandemic visit.

Table A2

Comparison of all-cause mortality rates during the COVID-19 pandemic vs before in a cohort of adults (*n* = 1630) who have injected drugs – participants with at least one study visit.

	Died Pre-Pandemic		Died During Pandemic		Incidence Rate Ratio, Pre- vs During Pandemic	
	Count	per 1000 person-years	Count	per 1000 person-years	Crude	Adjusted
All	243	39.0	48	42.1	1.08 (0.79–1.47)	1.09 (0.71–1.68)
Age Group						
18–49	64	27.2	16	30.8	1.13 (0.65–1.95)	1.08 (0.53–2.22)
50–59	127	45.1	25	54.6	1.21 (0.79–1.86)	1.15 (0.61–2.16)
60+	52	48.5	7	43.3	0.89 (0.41–1.97)	0.94 (0.31–2.88)
Gender						
Male	167	39.5	31	39.9	1.01 (0.69–1.48)	1.05 (0.62–1.78)
Female	76	37.8	17	46.7	1.24 (0.73–2.09)	1.31 (0.6–2.85)
Race						
Not Black	46	36.8	14	48.2	1.31 (0.72–2.38)	1.30 (0.59–2.84)
Black	197	39.5	34	40.0	1.01 (0.70–1.46)	1.06 (0.63–1.8)
Education						
Less than high school	140	41.8	27	45.7	1.09 (0.72–1.65)	1.21 (0.66–2.19)
High school or more	103	35.6	21	38.2	1.07 (0.67–1.72)	1.03 (0.54–1.96)
Recruitment Cohort						
All other recruitment waves	173	38.6	35	52.6	1.36 (0.95–1.96)	1.42 (0.80–2.51)
2015–2018	70	39.8	13	27.4	0.69 (0.38–1.24)	0.72 (0.35–1.49)
Any illicit drug Use						
No illicit drug use	97	35.4	19	41.6	1.18 (0.72–1.92)	1.20 (0.58–2.49)
Marijua-only	10	38.2	2	34.2	0.90 (0.20–4.09)	1.19 (0.12–11.82)
Illicit drugs, no injecting	42	38.0	14	61.1	1.61 (0.88–2.94)	1.60 (0.63–4.06)
Injected drugs	94	44.1	13	32.8	0.74 (0.42–1.33)	0.81 (0.39–1.69)
Any cigarettes						
No	39	28.5	9	37.8	1.33 (0.64–2.74)	1.22 (0.42–3.57)
Yes	204	41.9	39	43.2	1.03 (0.73–1.45)	1.09 (0.68–1.76)
Any alcohol						
No	117	36.6	19	31.9	0.87 (0.54–1.41)	0.86 (0.45–1.64)
Yes	126	41.5	29	53.3	1.29 (0.86–1.93)	1.38 (0.76–2.51)
Elevated depressive symptoms						
No	182	40.9	32	39.7	0.97 (0.67–1.41)	1.01 (0.60–1.70)
Yes	61	34.1	16	47.9	1.41 (0.81–2.44)	1.36 (0.62–2.98)
Employed						
No	224	42.6	44	45.6	1.07 (0.77–1.48)	1.11 (0.70–1.75)
Yes	19	19.4	4	22.9	1.18 (0.40–3.46)	1.14 (0.25–5.15)
Homeless						
No	218	40.6	38	40.0	0.98 (0.70–1.39)	1.00 (0.62–1.63)
Yes	25	28.7	10	52.9	1.84 (0.89–3.84)	1.66 (0.62–4.44)
HCV Ab+						
No	28	21.2	12	45.4	2.14 (1.09–4.21)	2.03 (0.74–5.61)
Yes	215	43.7	36	41.1	0.94 (0.66–1.34)	0.96 (0.59–1.55)
HIV Ab+						
No	158	35.4	35	42.0	1.19 (0.82–1.71)	1.18 (0.70–1.97)
Yes	85	47.9	13	42.3	0.88 (0.49–1.58)	0.93 (0.41–2.13)
Obese						
No	179	40.7	35	43.9	1.08 (0.75–1.55)	1.15 (0.69–1.92)
Yes	64	34.8	13	38.0	1.09 (0.60–1.98)	1.00 (0.44–2.27)
Number of chronic comorbidities						
0	74	34.3	11	27.4	0.80 (0.42–1.50)	0.81 (0.36–1.84)
1	64	32.9	21	61.2	1.86 (1.13–3.04)	1.83 (0.85–3.97)
2	49	41.7	8	37.1	0.89 (0.42–1.88)	1.11 (0.37–3.32)
3+	56	58.1	8	44.6	0.77 (0.37–1.61)	0.76 (0.28–2.06)

[1]Adjusted analysis adjusted for age, gender, race, education, cohort, drug use, cigarette use, alcohol use, depressive symptoms, employment, homelessness, HCV status, HIV status, obesity, number of comorbidities using propensity score weighting (see Analytic Approach).

Table A3

Comparison of injury and poisoning mortality rates during the COVID-19 pandemic vs before in a cohort of adults (*n* = 1630) who have injected drugs – participants with at least one study visit.

	Died Pre-Pandemic		Died During Pandemic		Incidence Rate Ratio, Pre- vs During Pandemic	
	Count	per 1000 person-years	Count	per 1000 person-years	Crude	Adjusted
All	109	17.4721	18	15.7888	0.90 (0.55–1.49)	0.79 (0.41–1.52)
Age Group						
18–49	46	19.5808	10	19.2284	0.98 (0.50–1.95)	0.90 (0.38–2.15)
50–59	50	17.7542	8	17.4576	0.98 (0.47–2.07)	0.88 (0.31–2.48)
60+	13	12.115	0	0	0 (0–NaN)	0 (0–NaN)
Gender						
Male	82	19.3995	16	20.6106	1.06 (0.62–1.82)	0.94 (0.46–1.94)
Female	27	13.4221	2	5.49835	0.41 (0.10–1.72)	0.39 (0.07–2.14)
Race						
Not Black	35	27.9796	6	20.6547	0.74 (0.31–1.76)	0.71 (0.25–2.00)
Black	74	14.8367	12	14.125	0.95 (0.52– - 1.75)	0.95 (0.40–2.24)
Education						
Less than high chool	52	15.5355	11	18.6256	1.20 (0.63–2.30)	1.14 (0.45–2.88)
High school or more	57	19.714	7	12.7397	0.65 (0.29–1.42)	0.55 (0.21– - 1.44)
Recruitment Cohort						
All other recruitment waves	66	14.7373	11	16.5341	1.12 (0.59–2.12)	1.16 (0.45–3.00)
2015–2018	43	24.4305	7	14.7445	0.6 (0.27–1.34)	0.58 (0.23–1.50)
Any illicit drug Use						
No illicit drug use	33	12.0471	5	10.9593	0.91 (0.36–2.33)	0.76 (0.22–2.64)
Marijua- only	4	15.2606	0	0	0 (0–NaN)	0 (0–NaN)
Illicit drugs, no injecting	18	16.2929	5	21.8211	1.34 (0.50–3.61)	1.15 (0.29–4.64)
Injected drugs	54	25.3236	8	20.1917	0.80 (0.38–1.68)	0.77 (0.31–1.96)
Any cigarettes						
No	13	9.50536	2	8.40786	0.88 (0.20–3.92)	0.74 (0.10–5.29)
Yes	96	19.709	16	17.7349	0.90 (0.53–1.53)	0.81 (0.41–1.61)
Any alcohol						
No	44	13.7516	10	16.7694	1.22 (0.61–2.42)	0.94 (0.38–2.34)
Yes	65	21.3893	8	14.7134	0.69 (0.33–1.43)	0.66 (0.26–1.67)
Elevated depressive symptoms						
No	77	17.313	14	17.3656	1.00 (0.57–1.77)	0.88 (0.41–1.89)
Yes	32	17.8669	4	11.9812	0.67 (0.24–1.9)	0.59 (0.16–2.09)
Employed						
No	98	18.6313	16	16.5758	0.89 (0.52–1.51)	0.80 (0.40–1.61)
Yes	11	11.241	2	11.4427	1.02 (0.23–4.59)	0.77 (0.11–5.31)
Homeless						
No	91	16.9564	14	14.7233	0.87 (0.49–1.52)	0.78 (0.37–1.65)
Yes	18	20.6462	4	21.1445	1.02 (0.35–3.03)	0.89 (0.24–3.33)
HCV Ab+						
No	19	14.3929	7	26.4674	1.84 (0.77–4.37)	1.48 (0.45–4.93)
Yes	90	18.2985	11	12.5632	0.69 (0.37–1.28)	0.62 (0.28–1.36)
HIV Ab+						
No	80	17.9151	13	15.6167	0.87 (0.49–1.57)	0.74 (0.35–1.56)
Yes	29	16.3562	5	16.2547	0.99 (0.38–2.57)	1.01 (0.26–3.90)
Obese						
No	81	18.4074	15	18.8077	1.02 (0.59–1.77)	0.93 (0.45–1.95)
Yes	28	15.2329	3	8.75906	0.58 (0.17–1.89)	0.45 (0.11–1.88)
Number of chronic comorbidities						
0	44	20.4104	7	17.4347	0.85 (0.38–1.90)	0.78 (0.28–2.15)
1	29	14.9241	5	14.5678	0.98 (0.38–2.52)	0.85 (0.24–2.98)
2	17	14.4681	3	13.8973	0.96 (0.28–3.28)	1.17 (0.19–7.20)
3+	19	19.6971	3	16.717	0.85 (0.25–2.87)	0.67 (0.14–3.20)

[1]Adjusted analysis adjusted for age, gender, race, education, cohort, drug use, cigarette use, alcohol use, depressive symptoms, employment, homelessness, HCV status, HIV status, obesity, number of comorbidities.

Table A4

ICD-10 Codes present in study sample by analytic cause of death category.

Cause of Death Category	ICD-10 Codes Present in Study Sample
Chronic	B182;C099;C140;C159;C189;C220;C229;C259;C329;C349;C445;C479;C509;C56;C61;C64;C679;C719;C787;C793;C80; C859;C900;D868;E112;E141;E142;E144;E145;E147;E149;E854;F019;F03;I078;I10;I119;I120;I219;I250;I251;I340;I420; brI429;I469;I48;I499;I500;I516;I632;I64;I672;I678;I739;I779;I839;J439;J440;J441;J449;J47;J81;K255;K703;K709;K729; K746;K769;N185;N19
Infectious	A047;A048;A419;A499;B201;B203;B207;B208;B218;B219;B220;B222;B227;B232;B238;B24;C539;I38;J110;J123;J151; J154;J189;J841;K659;M866;M869
Injury or Poisoning	F101;F109;F111;F191;F199;V031;V041;V092;V194;V196;V877;V892;W01;W10;W18;W19;X00;X42;X44;X599;X70;X74; X95;X97;X99;Y09;Y11;Y12;Y14
Other Causes of Death Occurring in This Cohort	E46;E785;E872;E877;E889;G931;G934;I613;I619;I629;I710;J690;K567;K631;K635;K819;K859;K922;NA;O961;R99
COVID-19	U071

Table A5
Standardized mean difference between pandemic and pre-pandemic person periods with and without propensity score weighting adjustment.

Covariate	All Cohort Members		Cohort with Study Visits	
	Unadjusted	Adjusted	Unadjusted	Adjusted
18–49	0.047	0.005	0.122	0.029
50–59	−0.051	−0.022	−0.083	−0.021
60+	0.004	0.018	−0.039	−0.008
Female	−0.033	0.000	−0.008	−0.001
Black	−0.088	0.000	−0.100	0.000
High school or more	0.013	−0.001	0.028	0.000
2015–2018	0.035	−0.001	0.178	0.000
No illicit drug use			−0.061	0.000
Marijuana only			0.004	0.000
Illicit drugs, no injecting			0.017	−0.001
Injected drugs			0.039	0.001
Used Cigarettes			0.022	0.001
Used Alcohol			−0.009	−0.001
Had Elevated Depressive Symptoms			0.021	0.000
Was Employed			0.001	0.000
Was Homeless			0.061	0.000
Was HCV Ab+			−0.032	−0.001
Was HIV Ab+			−0.033	−0.001
Was Obese			0.002	0.000
0 Chronic Conditions			0.026	0.000
1 Chronic Conditions			−0.009	0.000
2 Chronic Conditions			−0.010	0.000
3+ Chronic Conditions			−0.006	−0.001

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