A modified two-process Knox test for investigating the relationship between law enforcement opioid seizures and overdoses

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Recent research has shown an association between monthly law enforcement drug seizure events and accidental drug overdose deaths using cross-sectional data in a single-state, whereby increased seizures correlated with more deaths. In this study we conduct statistical analysis of street-level data on law enforcement drug seizures, along with street-level data on fatal and non-fatal overdose events, to determine possible micro-level causal associations between opioid-related drug seizures and overdoses. For this purpose we introduce a novel, modified two-process Knox test that controls for self-excitation to measure clustering of overdoses nearby in space and time following law enforcement seizures. We observe a small, but statistically significant ($p < .001$), effect of 17.7 excess non-fatal overdoses per 1000 law enforcement seizures within 3 weeks and 250 meters of a seizure. We discuss the potential causal mechanism for this association along with policy implications.

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1. Introduction

Law enforcement efforts to disrupt drug markets can cause those who have developed a dependency to the seized substances to shift to alternative dealers or different substances to maintain use and avoid withdrawal [8]. Overdose can occur when users are unaware of their tolerance, or unaware of the actual content of the new substances [14,23,50], which increases the likelihood of an overdose [4,22,26,34,35,38,51]. And while there are several studies that suggest drug seizures have no measurable public health benefit [2,15,55,56], only one recent study has attempted to empirically examine the relationship between law enforcement seizures and overdose [59]. This study by Zibbell and colleagues' found that fentanyl seizures in Ohio were associated with opioid-involved overdose deaths; however, causal inference was limited due to the data being aggregated and cross-sectional.

In the current study we analyze the space-time co-occurrence of seizure events of illicit opioids by law enforcement and opioid-related overdose events, all measured at the address level. We approach the problem from a point process perspective, where we consider the seizures and overdoses to be two separate processes and our goal is to assess their dependence. For this purpose a two process Knox test for clustering [27] can be used when the parent process intensity is separable. However, both law enforcement event data [37] and overdose event data [31] can exhibit self-excitation. In this situation, permutation of event times changes the second-order statistics of the process and the standard two process Knox test is no longer valid, as we will show in subsequent sections. To overcome this issue, we introduce a modified two process Knox test that uses a self-exciting point process, rather than a Poisson process, as the null distribution for the parent process. We then apply the test to assess the space-time relationship between law enforcement drug seizure events and opioid overdoses in a dataset from Indianapolis, Indiana covering 2014-2018.

The outline of the paper is as follows. In Section 2, we provide an overview of the standard Knox test, self-exciting point processes, and our modified Knox test. In Section 3, we describe the data used in our study. We analyze both non-fatal opioid-related overdose events, measured through emergency medical services (EMS) naloxone administrations, and coroner's data on accidental drug overdose deaths, both of which were collected in the same jurisdiction as law enforcement drug seizure events, over a five-year period in Indianapolis, Indiana. In Section 4, we present results from both a synthetic experiment illustrating the need for a modified two process Knox test and from an experiment applying the new two process test to coupled seizure-overdose data in Indianapolis. We observe a small, but statistically significant ($p < 10^{-3}$), effect of 17.7 excess non-fatal overdoses per 1000 law enforcement seizures within 3 weeks and 250 meters of a seizure. In Section 5, we discuss the policy implications of our findings.

2. Methodology

We consider a two-process Knox test [27,57] to detect excess clustering of overdoses following law enforcement drug seizures. In particular, given a time cutoff τ and spatial distance cutoff δ, the Knox statistic [28] $\kappa(\tau, \delta)$ is given by,

$$\kappa(\tau, \delta) = \sum_{i,j} 1\{\|\mathbf{x^o}_i - \mathbf{x}_j^s\| \le \delta, |t_i^o - t_j^s| < \tau\}. \tag{2.1}$$

Here the parent process, $\mathcal{D}^s = (\mathbf{x}_j^s, t_j^s)$, consists of the space-time drug seizure events and the dependent process, $\mathcal{D}^o = (\mathbf{x}_j^o, t_j^o)$, consists of the space-time overdose events. The Knox statistic counts the number of overdose events within a radius δ and within τ days of a drug seizure.

To determine excess clustering, the Knox statistic can be compared to a null hypothesis where the two processes are independent. If the parent process, $\mathcal{D}^s$, is Poisson or separable in time, then the process is invariant under a random permutation of the event times. Thus the null Knox

statistic and its uncertainty can be computed through multiple realizations of,

$$\widetilde{\kappa}(\tau, \delta) = \sum_{i,j} 1\{\|\mathbf{x^o}_i - \mathbf{x}_j^s\| \le \delta, |t_i^o - \widetilde{t}_j^s| < \tau\}, \tag{2.2}$$

where $\widetilde{t}_i^s$ are a random permutation of the event times of the drug seizure events.

In cases where the parent process, $\mathcal{D}^s$, is non-Poisson and exhibits self-excitation, then the permutation test is no longer valid [16]. We propose in this situation to use the following modified two-sample Knox test: 1) fit a self-exciting Hawkes process, $\mathcal{H}^s$, to the parent process, $\mathcal{D}^s$, that accounts for potential space-time clustering in the parent process itself and 2) calculate a bootstrap distribution for the null Knox statistic,

$$\widetilde{\kappa}^H(\tau, \delta) = \sum_{i,j} 1\{\|\mathbf{x^o}_i - \mathbf{z}_j^s\| \le \delta, |t_i^o - u_j^s| < \tau\}, \tag{2.3}$$

through repeated simulation of the Hawkes process. Here $(\mathbf{z}^s, u^s)$ are synthetic drug seizure event datasets with the same first and second order statistics as the original parent process.

To better disentangle the time-ordering between drug seizures and overdose events, we also analyze pre-post Knox statistics of the form:

$$\widetilde{\kappa}_\Delta(\tau, \delta) = \widetilde{\kappa}_1(\tau, \delta) - \widetilde{\kappa}_1(-\tau, \delta), \tag{2.4}$$

where

$$\widetilde{\kappa}_1(-\tau, \delta) = \sum_{i,j} 1\{\|\mathbf{x^o}_i - \mathbf{x}_j^s\| \le \delta, -\tau < t_i^o - \widetilde{t}_j^s < -1\}. \tag{2.5}$$

Because the time of occurrence of events in the data is uncertain (and hence the order of occurrence within the same day is uncertain), we include a 1-day buffer around drug seizures in Equation 2.5. A statistically significant positive value of $\widetilde{\kappa}_\Delta$ indicates that more overdose events cluster after a law enforcement drug seizure, whereas a statistically significant negative value would indicate a deterrence effect of the law enforcement intervention. We also compute an analogous pre-post Knox difference statistic, $\widetilde{\kappa}^H$, with the Hawkes process null replacing the random time permutation null model.

(a) Details of the Hawkes process null model

We fit a self-exciting Hawkes process [31] to drug seizure events with intensity,

$$\lambda(\mathbf{z}, u) = \mu f(\mathbf{z}) h_d(u) h_m(u) h_y(u) + \tag{2.6}$$
$$\sum_{u > u_i} \theta g_t(u - u_i; \omega) g_x(\mathbf{z} - \mathbf{z}_i; \sigma).$$

Here the background Poisson rate of events is assumed separable in space and time, where $f(\mathbf{z})$ models the spatial component of the background rate, fit using a Gaussian mixture model (GMM), and h_d, h_m, and h_y model day of the week, monthly, and yearly trends in the background rate. The second term in Equation 2.6 models self-excitation, where θ is the expected number of offspring events triggered by an event (under the branching process representation of the Hawkes process [52]), the temporal component g_t is assumed exponential, and the spatial component g_x is assumed Gaussian. The model is fit to the data using an expectation-maximization algorithm as detailed in [31,52]. We use residual analysis in Section 4 below to show goodness of fit of the model.

To construct confidence intervals for the Hawkes process null Knox statistics, $\widetilde{\kappa}^H$ and $\widetilde{\kappa}_\Delta^H$, we simulate multiple realizations of the Hawkes process fit to drug seizure data. The branching process representation of the Hawkes process is used for simulation, where first background Poisson events are generated from the Poisson process intensity $\mu f(\mathbf{z}) h_d(u) h_m(u) h_y(u)$. Offspring events are then iteratively added to the dataset, where each event generates $L \sim Pois(\theta)$ offspring events with spatial coordinates determined by adding random numbers drawn from g_x to the parent event location and a random number drawn from g_t to the time of the parent event.

To better match the spatial distribution of events in the actual data, which lie on a street network, we resample the original dataset coordinates using the EM estimation branching probabilities to assign spatial locations to the background events in each simulation.

3. Data Sources
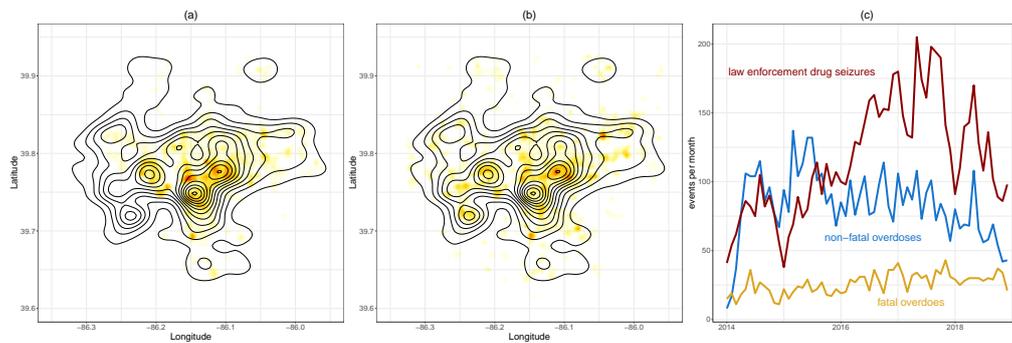
Figure 1. Association between law enforcement drug seizures and overdoses in Indianapolis. (a) Heat map of spatial distribution of non-fatal overdoses where EMS administered naloxone along with contour map of opioid-related law enforcement drug seizures in Indianapolis (2014 to 2018). (b) Heat map of spatial distribution of fatal overdoses along with contour map of opioid-related law enforcement drug seizures in Indianapolis (2014 to 2018). (c) Number of opioid-related law enforcement drug seizures per month (red), non-fatal overdoses where EMS administered naloxone per month (blue) and fatal overdoses in Indianapolis per month (orange).

Data for this study come from Indianapolis, Indiana, in Marion County, and cover January 1, 2014 through December 31, 2018. These data come from the property room and consist of the location, date, and physical description of the evident drug type seized by the metropolitan police department which covers over 90% of the county geographically. Because our indicator of time for the seizure events was limited to day (without time) we did not include overdose events that might have occurred on the same day of the seizure; offering a more conservative measure of the causal impact. Between 2014 - 2018, there were 6,201 individual opioid related drug seizures during 5,045 events, with an average of 1,240.2 per year (see Figure 1).

Toxicology data from Marion County, Indiana were used to measure fatal overdose events in this study. These data have been used to examine trends in fatal overdose events [9,40,41,43] and document gaps in the death investigation process [21,32]. Between 2014-2018, there were 1,626 fatal overdoses with the peak number occurring in 2017 with 406 deaths. Across this study period 85 percent of the overdose deaths were opioid-related; however we did not distinguish between these in the present analysis.

Non-fatal overdose data come from Indianapolis Emergency Medical Services which also covers nearly all of the county geographically and includes measures of naloxone administration and calls for overdose events [42]. The records database for EMS events includes where the event occurred, the chief complaint, and whether naloxone was administered to the patient. There were 7,228 total naloxone administrations with an average of 1,445.6 administrations per year.

## 4. Results

In this section we first conduct a synthetic experiment to illustrate the need for a modified two-process Knox test. We then estimate a Hawkes process model from the Indianapolis data and assess the goodness of fit of the model. Finally, we apply the modified Knox test to the coupled seizure-overdose data to assess co-clustering of the two processes.

## (a) Synthetic experiment illustrating failure of standard two-process Knox statistic under self-excitation

To illustrate the need for a modified Knox test, we simulate two independent Hawkes processes, each with parameters $\theta = .75$, $\omega = .1$, $\sigma = .01$ and background rate specified as in Equation 2.6 with day of week marginal density $h_d \propto [1, 2, 3, 4, 3, 2, 1]$, month of year marginal density $h_m \propto [3, 3, 4, 4, 5, 6, 6, 5, 4, 4, 3, 3]$, yearly trend density $h_y \propto [2, 3, 4, 5]$ and $\mu = 500/(4 \cdot 365)$. For the spatial component of the background rate we specify a Gaussian mixture model with 3 components having means $m_1 = [.2, .7]$, $m_2 = [.5, .5]$, $m_3 = [.7, .2]$, diagonal covariance matrices $diag(\Sigma_1) = [.01, .01]$, $diag(\Sigma_2) = [.025, .09]$, and $diag(\Sigma_3) = [.04, .0004]$ and mixture probabilities $p_1 = .2$, $p_2 = .5$ and $p_3 = .3$.

In Figure 2, we compare the permutation based Knox test, where the parent process times are repeatedly permuted to construct a bootstrap distribution for κ, with a modified Hawkes process based Knox test, where 1) the Hawkes process parameters are estimated from the parent process using an EM algorithm and 2) bootstrap replicates of the parent process are obtained by repeatedly sampling realizations from the estimated Hawkes process parameters. We observe that the permutation based Knox statistic distribution has too small of variance and does not contain the observed Knox statistic of the original two independent processes within its range (after 250 bootstrap samples). On the other hand, the Knox statistic for the original data is well contained within the 95% bootstrap confidence interval under the Hawkes process null.
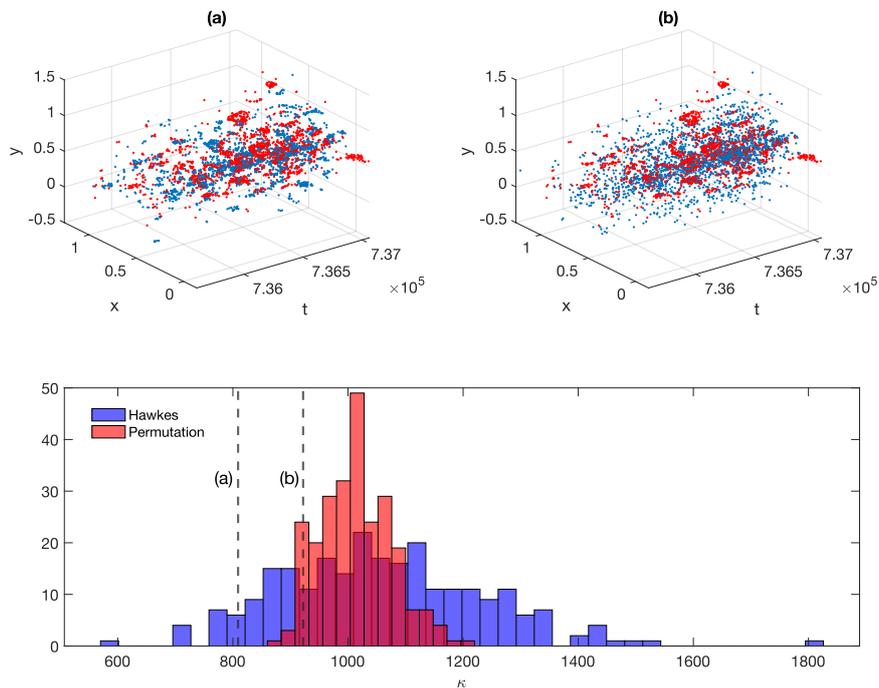
Figure 2. Top: (a) two simulated independent Hawkes processes and (b) the same two simulated Hawkes processes with the parent process (blue) times randomly permuted. The time range is specified as 2013 to 2016 and is displayed, by Matlab convention, in units of days since Jan 0, 0000. Bottom: Knox statistic bootstrap distribution for the standard permutation based Knox test (red) and for the modified Hawkes process based Knox test (blue). The dashed lines represent the Knox statistics obtained for the two simulated datasets above (e.g. the "real" dataset in the case of (a) and data after permutation of the parent process times in (b)).

## (b) Estimation of the Hawkes process from drug seizure data
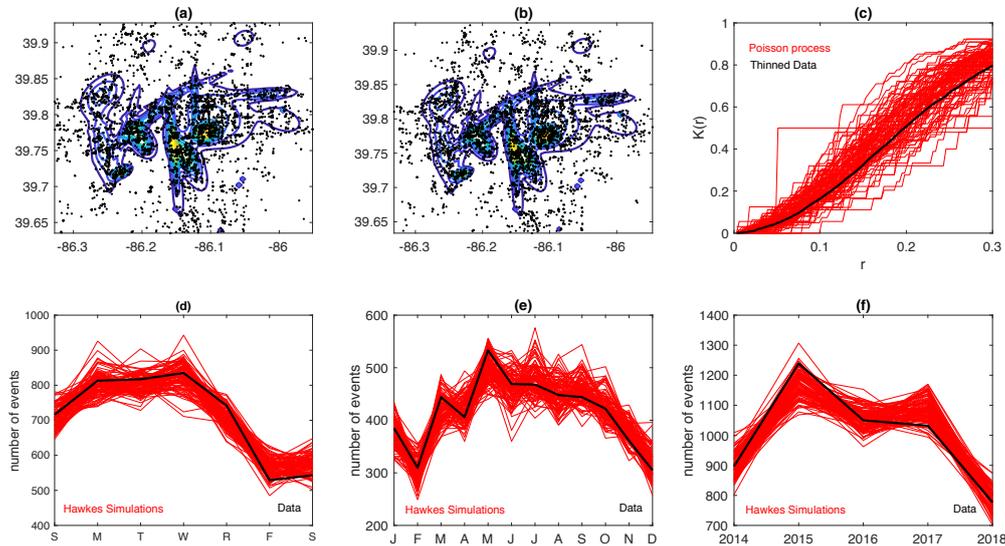
Figure 3. Hawkes process fit to drug seizure data. (a) Scatter plot of drug seizure data coordinates along with GMM background intensity estimate contour plot for a fitted Hawkes process ($\hat{\theta} = 0.239$, $\hat{\omega} = 2.306$, and $\hat{\sigma} = 0.006$). (b) Scatter plot of event coordinates of one realization of a simulated Hawkes process fit to drug seizure data. (c) K-function (black) of fitted Hawkes process thinned residuals of the drug seizure data (thinned with probability $\lambda_{inf}/\lambda(t_i)$). K-function for 100 realizations of a constant rate Poisson process (red). Radius r measured in degrees. (d-f) Distribution of number of events per day (d), per month (e) and per year (f) for law enforcement drug seizure data (black) and 100 fitted Hawkes process simulations (red).

Next we fit the Hawkes process model in Equation 2.6 to law enforcement drug seizure data in Indianapolis. For the background rate we use a 20-component Gaussian mixture to model the spatial distribution of events, $f(\mathbf{z})$. In Figure 3 we display an example simulation from the fitted Hawkes process, along with the estimated model parameters and the background rate GMM components. To assess the goodness of fit, we apply residual analysis and thin the original drug seizure data by retaining events with probability $\lambda_{inf}/\lambda(\mathbf{x}_i^s, t_i^s)$ (where λ_{inf} is the infimum of the intensity on the domain of Indianapolis). When the model is correctly specified, the thinned residual points are a realization of a constant-rate Poisson process. In Figure 3 we display the K-function [44] (area normalized number of points within a given radius) for the thinned residuals along with the K-function of 100 simulated Poisson processes.

(c) Association between drug seizures and overdose in Indianapolis

Next we apply the standard permutation based Knox test and the modified Hawkes process Knox test to Indianapolis drug seizure and opioid overdose data. In Figure 4, we display the bootstrap null distribution corresponding to the standard (red) and Hawkes process (blue) pre-post tests. As an example, in Figure 4 we show the distances in time and space of subsequent overdoses relative to drug seizures within 250 meters and within 21 days, a spatial and temporal scale that yields $\kappa = 510$. In Figure 4, we also plot inter-event distances and the Knox statistic for example realizations of the permutation and Hawkes process null models, along with the distribution of the Knox statistics for $\tau = 21$ days and $\delta = 250$ meters.
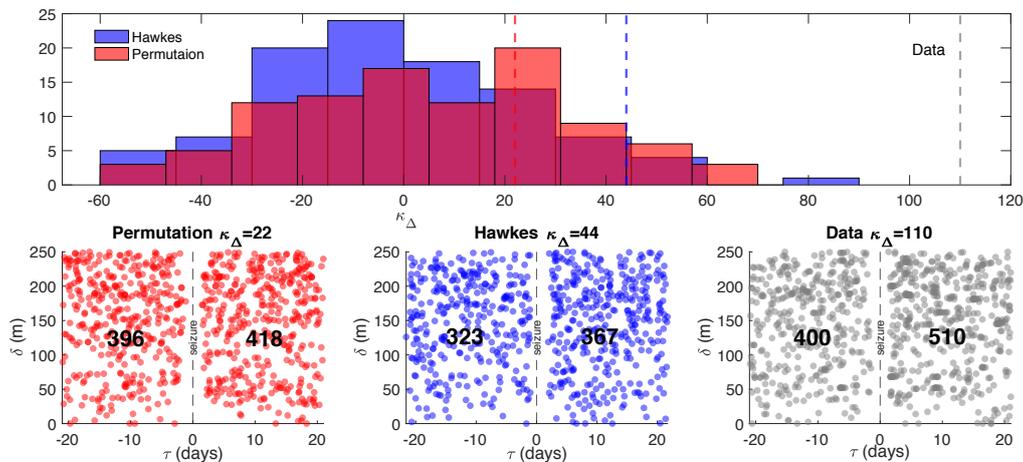
Figure 4. Top: Distribution of the pre-post Knox difference statistic, κ_Δ, for the permutation and Hawkes process null models applied to non-fatal overdoses within 21 days and 250 meters of a law enforcement drug seizure. Bottom: Distances in time and space of non-fatal overdoses are shown relative to drug seizures (with a 1 day buffer window removed) for an example realization of the permutation process (original seizure data with times reshuffled), an example realization of the Hawkes process fit to seizure data, and the actual observed data. In the observed data there are 510 overdose events within 250 meters and within 21 days following drug seizures compared to 400 overdose events within 250 meters and within 21 days preceding drug seizures. The null models are designed to control for day of week, seasonal, trend, and self-excitation effects that could lead to excess overdoses following drug seizures.

Next we use the permutation based two-process Knox test to investigate the effect of opioid-related law enforcement drug seizures on non-fatal overdoses where EMS administered naloxone (Figure 5a). We observe excess clustering of non-fatal overdose events around opioid-related drug seizures across a wide range of temporal and spatial cutoffs. For example, within 14 days and 500 meters of seizures, we expect a 95% confidence interval for $\widetilde{\kappa}$ of 1633 to 1800 overdose events (cumulative across all 14 day, 500 meter windows surrounding all drug seizures in the dataset); however, we observe 1928 events in those windows in the actual data, a statistically significant effect at the $p = .001$ level. In Figure 6a we display the analagous results for the Knox test using the Hawkes process null. Thought the confidence interval is wider when the Hawkes process null is used, we still find that the effect is statistically significant below the .001 level. This co-clustering is significant even when controlling for multiple comparisons (e.g. conservative Bonferroni correction).

In Figures 5b and 6b we also report results for the pre-post Knox difference tests applied to non-fatal drug overdoses. Here we observe a statistically significant increase in the number of non-fatal overdoses after an opioid-related law enforcement seizure compared to the same time period before and same spatial radius. The effect appears to be weaker farther away from the seizure event; however, for a relatively small radii (100-250 meters), we find statistically significant effects for both the Hawkes and permutation test. For example, within 21 days and 250 meters of seizures, under the null hypothesis we expect a 95% confidence interval of -53 to 68 for the difference in overdoses before and after a seizure event. However we observe a difference of 110 overdoses ($p = .001$), which corresponds to 17.7 excess overdoses within 21 days (after) and 250 meters per 1,000 seizures.

Finally, in Figures 5-6c and 5-6d we provide results for the 2-sample Knox tests when fatal overdoses are used as the unit of analysis. Here we find a statistically significant effect of fatal overdose clustering around seizures in the majority of the radii and temporal windows used (for both the permutation and Hawkes process nulls). However, we failed to detect any effect when

applying the pre-post Knox difference test, indicating that fatal overdoses fall temporally on either side of seizures with similar rates in the present data set. These results were replicated using only opioid-related overdose deaths, but again did not detect the pre-post seizure effect.
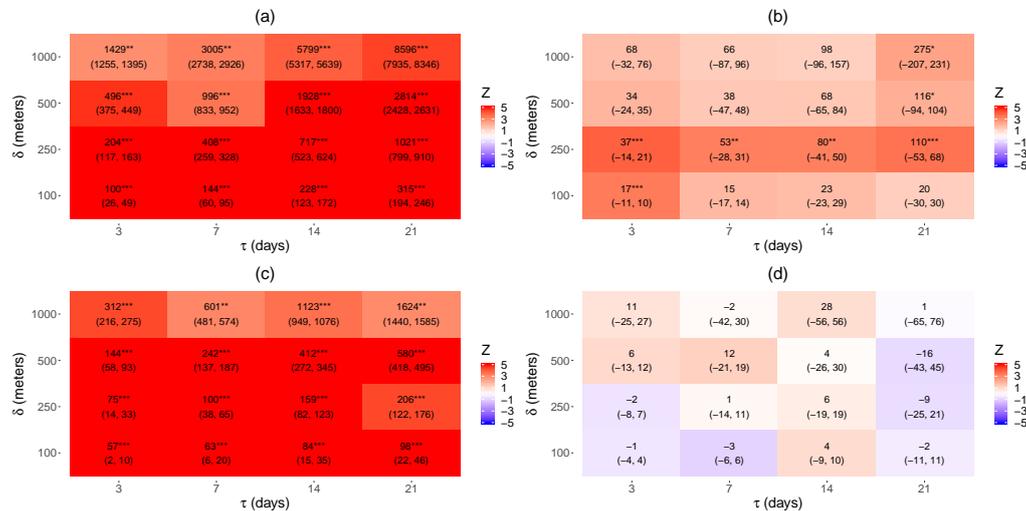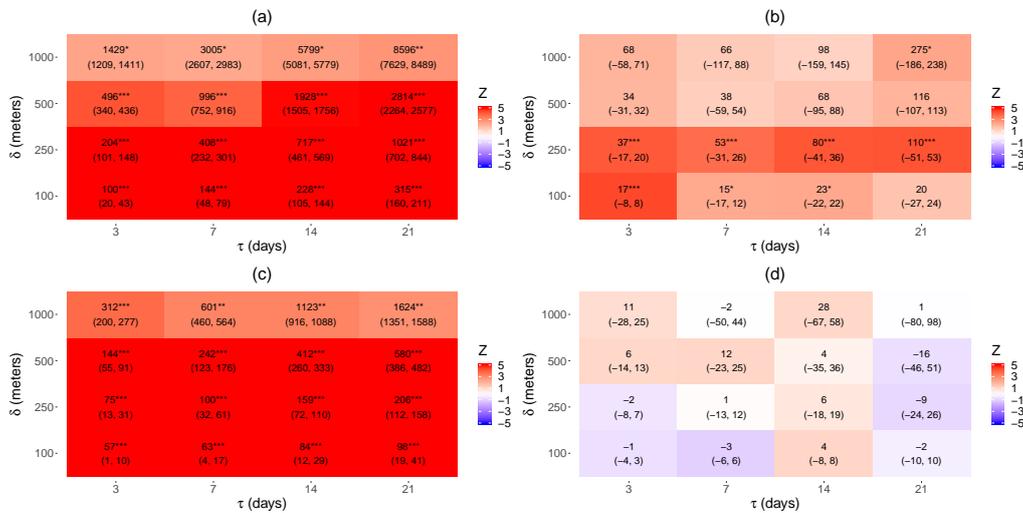

Figure 5. Knox permutation test statistics reported for varying spatial and temporal cutoffs δ and τ. (a) Knox test results for association between drug seizures and overdoses where naloxone was administered by EMS. Knox test statistic κ reported for the data along with 95% confidence intervals for the Knox statistic corresponding to the most conservative null model (Hawkes or Permutation). (b) Modified pre-post knox statistic κ_Δ reported for the non-fatal overdose data along with 95 % confidence interval. (c) Knox test results for association between drug seizures and fatal overdoses. Knox test statistic κ reported for the data along with 95% confidence interval. (d) Modified pre-post knox statistic κ_Δ reported for the fatal overdose data along with 95 % confidence interval. Significance level denoted by * (p=.05), ** (p=.01), and *** (p=.001) and color coded by the Z-value of the Knox test statistic (red indicating clustering and blue indicating inhibition).

5. Discussion

Using law enforcement drug seizure data, alongside both fatal and non-fatal overdose data for a 5-year period in the same jurisdiction, our analysis found statistically significant excess clustering of non-fatal overdoses, within a given time frame and spatial distance, following an opioid-related drug seizure event. These non-fatal overdoses are where EMS administered naloxone - the medication designed to rapidly reverse opioid overdose - and confirmed through multiple analysis that all suggest increases within the radius of an opioid-related law enforcement drug seizure.

A number of studies have documented how law enforcement disruptions to the local drug market can result in persons with a chemical dependency to the seized substances shifting to alternative dealers or using different substances [2,3,5,7,8,19,25,54,59]. Drug users can have a long-standing and trusting relationship with a supplier which often comes with consistency of a product quality [8]. In the case of opioids this could include either prescription medications (e.g., oxycodone, hydrocodone, oxymorphone, hydromorphone) or illicitly produced heroin and fentanyl where the shift to a new dealer or substance can be chaotic as the person will likely be attempting to avoid painful withdrawal symptoms [10,30,46]. Moreover, when using new or unknown products it is not possible to determine tolerance so it could be a more potent opioid, resulting in an overdose, or less potent, result in co-use with other substances and overdose.

Figure 6. Modified Knox Hawkes test statistics reported for varying spatial and temporal cutoffs δ and τ. (a) Modified Knox test results for association between drug seizures and overdoses where naloxone was administered by EMS. Knox test statistic κ reported for the data along with 95% confidence intervals for the Knox statistic corresponding to the most conservative null model (Hawkes or Permutation). (b) Modified pre-post knox statistic κ_Δ reported for the non-fatal overdose data along with 95 % confidence interval. (c) Modified Knox test results for association between drug seizures and fatal overdoses. Knox test statistic κ reported for the data along with 95% confidence interval. (d) Modified pre-post knox statistic κ_Δ reported for the fatal overdose data along with 95 % confidence interval. Significance level denoted by * (p=.05), ** (p=.01), and *** (p=.001) and color coded by the Z-value of the Knox test statistic (red indicating clustering and blue indicating inhibition).

On the other hand, we note that there are other possible explanations for excess clustering of overdoses following drug seizures.

While our study is limited to administrative data sources from a single jurisdiction and time period, it represents a critical step in understanding how law enforcement practices supported by current US drug policy may inadvertently aid the ongoing overdose epidemic. Future research should aim to replicate these results in other jurisdictions with similar data sources, but also look for alternative data sources, such as Zibbell and colleagues' use of crime laboratory data (2019), to look at the relationship between drug seizures and overdose events nationwide. Our results suggest an increase in non-fatal overdose following drug seizures but not fatal overdoses, which may be driven by demographic characteristics, drug use behaviors, or 911 call response [18,39], which were not accounted for in this study. Despite these limitations, the results highlight the importance of public health and police partnerships in addressing the opioid epidemic. Police can play an integral part in promoting public health, and this has occurred most recently in the overdose epidemic through training and co-response efforts for individuals with behavioral health concerns [6], violence prevention initiatives [29,33,48], and numerous multi-sector coalitions. Yet these results suggest the need for a rapid community response following a drug seizures; this response would need to target harm reduction and treatment opportunities to a specific geographical region. This idea aligns more with recent policing efforts that focus on harm reduction [36], arrest diversion programs [13], and police-led treatment initiatives for opioid use disorder [58], compared to traditional place-based deterrence policing methods. A police-public health collaboration following police drug seizures is also an opportunity to link individuals to treatment and lower the rate of overdoses.

There are also broader policy implications from the results in this study. The "war on drugs" has long been deemed a US policy failure, yet the vast majority of law enforcement agencies

continue to enact practices aimed at laws criminalizing illicit substances. The decriminalization reform efforts in Portugal started in 2001 have been wildly successful at reducing the burden of drug-related harms, with demonstrated decreases in overdose, HIV/STI, and incarceration [24]. Nearly 20 years later the question of whether decriminalization is politically feasible in the US has been answered with Oregon as the first US state to decriminalizes the possession for small amounts of cocaine, heroin, and methamphetamine beginning in 2021 [1,12,17]. This is also following a number of states that regulated of cannabis, suggesting a growing policy trend away from law enforcement responses. With the overdose epidemic being exasperated as part of a syndemic with COVID-19 [20,45,49,53], if the results from this study are replicable, then both local practices, along with state and federal policies, will need to transform to reduce preventable deaths and the continued loss of potential life in the US.

Finally, we believe that the modified Knox test introduced in this study will be useful in assessing co-clustering effects in other applications where two spatial-temporal point processes may interact. Future research may focus on handling other types of processes, for example self-correcting or self-avoiding point processes, where random permutation can change the statistics of the process and a modified null model is needed. These models can then be assessed using the residual analysis employed here or by alternative point process goodness-of-fit techniques, such as super-thinning [11]. We note that there is some tradeoff between the standard permutation test, that preserves spatial structure in the data (though may change the second order statistics), and our approach that introduces some spatial smoothing. While we resampled the event coordinates to address this concern, future research could also focus on designing modified Knox tests that better capture the spatial statistics of street networks [47].

6. Acknowledgements

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