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The salience of social context, opioid antagonist use, and prior opioid exposure as determinants of fatal and non-fatal opioid overdoses

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ABSTRACT

This study examines the salience of social context for opioid overdoses in Boston from 2014 to 2019. Longitudinal negative binomial models with random effects indicated that higher levels of concentrated disadvantage, residential instability, and illicit drug activity increased annual block group counts of opioid overdoses. Logistic hierarchical and cross-classified random effects models indicated that the use of Narcan and greater exposure to drugs through previous opioid overdose and contextual lillicit drug crime activity reduced the odds of fatal opioid overdose relative to non-fatal opioid overdose. The findings suggest that the accurate tracking of both fatal and non-fatal overdoses, and a consideration of the broader social context, can facilitate effective public health resource allocation to reduce opioid overdoses.

1. Background

The opioid epidemic remains a serious public health concern in the United States (Altekruse et al., 2020). The nature of the epidemic has shifted from prescription opioid overdoses in the late 1990s and early 2000s to overdoses involving heroin in the early 2010s, synthetic opioids such as fentanyl in the middle 2010s, and most recently the mixing of stimulants (such as cocaine and methamphetamine) intensified by mental illness comorbidities (Jenkins, 2021). Beyond these shifts in the characteristics of opioid overdoses, the annual number of opioid overdose deaths more than tripled from 21,000 in 2010 to 70,000 in 2020 (Ghose et al., 2022). Moreover, the COVID-19 pandemic exacerbated opioid overdose mortality rates: the age-adjusted rate of overdose deaths involving synthetic opioids other than methadone increased 56% from 11.4 per 100,000 in 2019 to 17.8 in 2020, eclipsing the 15% increase observed from 9.9 per 100,000 in 2018 to 11.4 in 2019 (Hedegaard et al., 2021a). All states have been impacted by the opioid epidemic, but the crisis is particularly acute in Massachusetts: in 2020, the opioid overdose fatality rate was over twice as high in Massachusetts than the national average (Massachusetts Department of Public Health, 2022).

The growing toll of the opioid epidemic warrants supply-controlling and harm-reduction policy interventions from all levels of government. However, the risk factors for opioid overdose that inform policy measures are not well understood (Doggui et al., 2021). Research has focused primarily on fatal opioid overdoses, which are linked to individual risk factors such as gender and race (Mathers et al., 2013) and synthetic opioids such as illicitly manufactured fentanyl (Latkin et al., 2019). Indeed, the proportion of fatal overdoses involving synthetic opioids other than methadone (e.g., fentanyl, fentanyl analogs, and tramadol) has increased annually since 1999, with the most intense growth observed between 2010 (14%) and 2020 (82%) (Hedegaard et al., 2021a). Fatal overdoses, however, represent just a small proportion of all opioid overdoses, and there are indications that fatal and non-fatal opioid overdoses have distinct etiologies (Bagley et al., 2019). Fatal opioid overdoses also tend to be preceded by non-fatal overdoses (Caudarella et al., 2016; Olfson et al., 2018), suggesting that the time period after non-fatal overdose is a critical opportunity for intervention. Unfortunately, studies examining the factors that distinguish fatal and non-fatal opioid overdoses are sparse.

Additionally, literature linking the broader social context to opioid use is nascent, although recent studies have examined the relevance of social context for opioid overdose. For example, examining statewide opioid overdose death data across census block groups in Rhode Island, Schell et al. (2022) found that overdose death was: inversely associated with educational attainment, residential stability, median housing values, and average household income; and positively associated with the proportion of the population living alone or unmarried. Using data on opioid overdose events in Columbus, Ohio, Yuchen et al. (2022)

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demonstrated that higher numbers of overdose events were positively associated with the percentage of residents living in poverty and the number of vacant housing units, and inversely associated with median household income and educational attainment. Additionally, areas with higher levels of perceived safety, wealth, and liveliness (as measured from Google Street View imagery) had lower numbers of opioid overdose events. Similarly, Pear et al. (2019) found elevated rates of prescription opioid overdose in more economically disadvantaged zip codes across 17 states, and Hollingsworth et al. (2017) demonstrated that U.S. counties and states with higher rates of unemployment had higher rates of opioid death and overdose emergency department visits.

Studies utilizing multilevel models have also linked contextual characteristics to individual variation in opioid overdose. Using 2011–2014 Massachusetts death certificate data, Flores et al. (2020) found that the percentage of the population living in poverty, food insecurity rate, number of health centers, and concentration of opioid prescriptions (in the form of hydromorphone) were positively associated with opioid-related premature deaths, relative to non-opioid-related mortality. Using the data from the Mortality Disparities in American Community Study (MDAC), Altekruse et al. (2020) demonstrated that opioid fatality was associated with indicators of low socioeconomic status. In a multilevel case control study of accidental overdose deaths and accidental deaths due to other causes across 59 New York City neighborhoods in 1996, Galea at el. (2003) found that the odds of overdose death were higher in neighborhoods with the least equitable income distribution.

It is also noteworthy that research has examined differences in the contextual predictors of opioid events across urban/rural context and race. Chichester et al. (2020) demonstrated that land use characteristics such as proximity to bus stops, public parks, and schools was positively associated with opioid overdose events in rural areas in Jefferson County, Alabama, while inpatient treatment centers, transitional living facilities, express loan establishments, and liquor vendors were positively associated with opioid overdose events in urban areas. In Chicago, Rushovich et al. (2022) found that the positive association between neighborhood economic hardship and opioid-related overdose death was pronounced among non-Hispanic whites. Among non-Hispanic blacks, rates of opioid-related overdose death were elevated in all neighborhood types, suggesting that black individuals living in more economically stable communities face additional challenges that may contribute to higher rates of opioid-related overdose deaths.

This nascent but growing body of research recognizes that the opioid epidemic is partially rooted in community characteristics such as: social inequality, including low educational attainment, low levels of household income, and impoverishment; economic distress, including social disorder (e.g., public consumption of alcohol, visible drug sales, adults fighting in public) and physical disorder (e.g., garbage or litter on streets and sidewalks, graffiti, abandoned cars); and underinvestment, or lack of investment in the built environment (e.g., road infrastructure, sidewalk attractiveness, presence of recreation sites and structures) (Yuchen et al. (2022). Moreover, "while existing predictive models that focus on overdose risk at an individual level can assist in clinical decision-making … [a] focus on neighborhood-level predictors is better suited to optimizing the allocation of public health resources and targeted community-focused interventions" (Schell et al., 2022, p. 529). Accordingly, we employ descriptive, spatial, and multilevel regression techniques to examine the salience of contextual characteristics for fatal and non-fatal opioid overdose in Boston from 2014 to 2019.

The first aim of this study is to examine the contextual correlates of area levels of opioid overdose. To accomplish this, longitudinal negative binomial models with random effects examine the contextual characteristics that predict annual block group counts of all (fatal and nonfatal) opioid overdoses. The second aim of the study is to examine the individual and contextual characteristics that differentiate fatal and non-fatal opioid overdoses. To this end, a series of *t*-tests and Chi-square tests for categorical data provide a descriptive comparison of the independent variables across fatal and non-fatal opioid overdoses. Logistic hierarchical and cross-classified random effects models then predict the odds of fatal opioid overdose relative to non-fatal opioid overdose with relevant event, person, census block group, and census tract factors.

2. Methods

2.1. Data

Two official data sources were combined to identify all known opioid overdose victims in Boston from 2014 to 2019. First, the Boston Public Health Commission (BPHC) provided data on 18,322 unique overdose (any drug) events involving 8855 overdose patients that occurred in Boston from 2014 to 2019 and resulted in an Emergency Medical Services (EMS) response. Second, the Commonwealth of Massachusetts Registry of Vital Records and Statistics (VRS) provided data on all 11,738 fatal drug-related overdoses that occurred in Massachusetts between August 30, 2014, and December 31, 2019. Because VRS data were unavailable prior to August 30, 2014, BPHC data were used to identify overdose fatalities during this time period.

The combined Boston EMS and Massachusetts VRS data resulted in a database of 19,609 drug-related overdoses in Boston from January 2014 to December 2019, of which 16,347 were single-victim, opioid-related overdoses that had valid person-level information. An iterative matching process based on names and birth dates was utilized to identify and link unique subjects across the two datasets. Cases that did not result in an exact match were linked by "fuzzy matching" techniques that accounted for variations in subjects' full and abbreviated names (e.g., "Nick" vs. "Nicholas"). These cases were manually reviewed to confirm the match to a probable degree of certainty.

Overdoses that did not have missing geographic identifiers or occur in empty (zero population) census-designated block groups or tracts were geocoded to latitude and longitude coordinates in ArcGIS v10.8 using the MassGIS address locator; unmatched addresses were geocoded through Geocodio and Google. Geocoded data were linked to census block group and tract information in the American Community Survey (ACS), a continuous nationwide survey of 3.0–3.5 million households in the U.S. Data were derived from the five-year period 2015–2019. The final sample consisted of 15,911 fatal and non-fatal opioid overdose events representing 8679 persons, 544 census block groups, and 173 tracts in Boston from 2014 to 2019.

2.2. Measures

Event characteristics included: whether (1 = yes; 0 = no) the overdose occurred on hospital property; whether Narcan was used during the event; and person age at time of event (under 30, 30–39, 40–49, and 50 or older). The analysis also controlled for year of overdose. The Narcan variable was based on the Boston EMS data, thereby accounting only for opioid overdoses that resulted in an emergency call to EMS. This variable was coded in the affirmative if Narcan was administered by: (1) a professional, including an Emergency Medical Technician (EMT), police officer, or firefighter; or (2) a bystander of acquaintance, but only if EMS responded to the scene and was informed that Narcan had been administered to the patient. This variable does not capture overdoses in which Narcan was administered by someone other than a professional when EMS was not contacted.

Person-level variables included: gender (male or female); race/ethnicity (white, African American, Hispanic, and other); and whether the opioid overdose victim had a history of opioid overdose. Research has documented these person-level factors as influential determinants of opioid overdose. For example, studies have highlighted the existence of racial and ethnic disparities in overdose mortality (Friedman et al., 2021; Khatri et al., 2021; Lippold et al., 2019; Moallef et al., 2022) and access to medications for opioid use disorder (Chunara et al., 2021;

Goedel et al., 2020; Kalmin et al., 2021; Nolen et al., 2022). Research has also demonstrated that individuals with a history of opioid overdose are at greater risk of subsequent fatal overdose (Caudarella et al., 2016; Mathers et al., 2013; Olfson et al., 2018).

Census block group and census tract factors included: population (divided by 100); racial/ethnic heterogeneity; residential instability; concentrated disadvantage; and illicit drug activity. Heterogeneity was measured using Blau's index by summing the squared proportion of the population in each racial/ethnic group and then subtracting this sum from one ($1 - \sum p_i^2$). Residential instability was measured as the standardized sum of two items: (1) the proportion of the population renting their homes; and (2) the proportion of the population that moved between 2015 and 2018. Concentrated disadvantage was calculated as a weighted factor regression score of: proportion of the population aged 18–64 living below the poverty line; proportion of the civilian workforce unemployed; proportion of single female-headed households with children; proportion of the population receiving some form of public assistance; average household value; and proportion of the population aged 25 and older with a high school degree (last two items reverse-coded). This is a well-established scale with well-documented validity and internal consistency reliability (Messer et al., 2006; Sampson et al., 1997). Illicit drug activity was measured as the count of Boston Police Department drug crime arrests.

2.3. Analytic approach

Grounded in the study aims, the analysis proceeds in two stages. The first stage of analysis seeks to unravel the effects of socio-structural characteristics on areal opioid overdoses. To this end, longitudinal negative binomial models with random effects predict annual block group counts of all opioid overdoses. The unit of analysis is a block group-year ($N = 544$ block groups × 6 years = 3264 block group-years). These models are ideal for analyzing count data as they correct for the over-dispersion of a skewed distribution (Long and Freese, 2006) and are especially well suited for analyzing rare events (Osgood, 2000) such as opioid overdoses. Population is included in all models, effectively modelling rates.

The second stage of analysis utilizes a series of t-tests and Chi-square tests for categorical data to provide a descriptive comparison of the event, person, and contextual characteristics across fatal and non-fatal opioid overdoses. Multilevel models then examine the event, person, and contextual characteristics that impact the odds of fatal opioid overdose relative to non-fatal opioid overdose. Of the 8679 persons in the sample, 6033 (69.51%) were involved in one opioid overdose event, while 2646 (30.49%) were involved in at least two events. The mean number of opioid overdose events per person was 1.83; there were 15.95 persons, on average, nested within each census block group, and 50.17 persons per census tract. This created a data structure in which the 15,911 opioid overdose events were nested within the 8679 sample persons *and* 544 census block groups; in turn, census block groups were nested within 173 census tracts. This necessitated the use of a three-level hierarchical and cross-classified random effects model, in which opioid overdose events at level-1 were cross-classified by persons and census block groups at level-2, and block groups were nested within census tracts at level-3. The model was estimated in *HLM 8.00* with a binary outcome indicating a fatal opioid overdose (unity) versus a non-fatal opioid overdose (zero). Appendix A provides full equations for the unconditional and fully specified models.

3. Results

3.1. Predicting areal opioid overdoses

Table 1 presents the longitudinal negative binomial models with random effects predicting counts of opioid overdoses across Boston block groups from 2014 to 2019. Model 1 indicates that concentrated disadvantage (IRR = 1.12, 95% CI = 1.03,1.22), racial/ethnic heterogeneity (IRR = 1.70, 95% CI = 1.08,2.69), and residential instability (IRR = 1.17, 95% CI = 1.08,1.28) were positively associated with opioid overdoses. Model 2 adds drug crime arrests to account for block group illicit drug activity. The results indicate that block groups with more illicit drug activity had elevated counts of opioid overdoses (IRR = 1.07, 95% CI = 1.06,1.08). The results pertaining to concentrated disadvantage and residential instability persist after controlling for drug crime arrests, but the effect of racial/ethnic heterogeneity is reduced to non-significance.

Table 1
Predicting annual block group counts of opioid overdoses, $N = 3264$ block group-years.

Variable	Model 1		Model 2	
	IRR	95% CI	IRR	95% CI
Population	1.03***	[1.01, 1.04]	1.02**	[1.01, 1.03]
Concentrated Disadvantage	1.12**	[1.03, 1.22]	1.11**	[1.03, 1.19]
Racial/Ethnic Heterogeneity	1.70*	[1.08, 2.69]	1.20	[.80, 1.81]
Residential Instability	1.17*	[1.08, 1.28]	1.18***	[1.10, 1.27]
Drug Crime Arrests			1.07***	[1.06, 1.08]
Intercept	3.12***	[2.31, 4.21]	2.72***	[2.08, 3.56]

Abbreviations: IRR = incidence rate ratio; CI = confidence interval.
Notes: A one unit change in block group population represents 100 persons.
$^{*}p < .05$, $^{**}p < .01$, $^{***}p < .001$ (two-tailed tests).

3.2. Comparing the characteristics of opioid overdoses across fatal and non-fatal overdoses

Table 2 provides a description comparison of the event, person, census block group, and census tract characteristics across the 1354 fatal and 14,557 non-fatal opioid overdoses in Boston from 2014 to 2019. Regarding the event characteristics, significantly more fatal overdoses (27.18%, $n = 368$) than non-fatal overdoses (1.33%, $n = 193$) occurred on hospital property. Fatal overdoses were significantly less likely to involve the use of Narcan (10.56%, $n = 143$) than non-fatal overdoses (53.68%, $n = 7814$). Less than half of fatal overdoses involved persons under 40 years of age (47.27%, $n = 640$), whereas more than half of non-fatal overdoses involved persons under 40 (56.90%, $n = 8283$). While non-fatal opioid overdoses increased throughout the study period, fatal opioid overdoses increased annually from 2015 to 2017 and subsequently decreased, aligning with the nationwide decrease in fatal opioid overdoses reported during 2018 (Hedegaard et al., 2021a). Additionally, the proportion of overdoses that were fatal decreased from 10.63% in 2015 to 10.14% in 2016, 9.08% in 2017, 7.75% in 2018, and 7.24% in 2019. This is due, in part, to significant changes in naloxone prescription dispensing after 2017 (CDC, 2022a).

With respect to the person-level factors, similar percentages of males were involved in fatal (74.74%, $n = 1012$) and non-fatal (72.91%, $n = 10{,}613$) overdoses; and fatal and non-fatal overdoses were distributed comparably across race/ethnicity. Fewer fatal overdoses (26.96%, $n = 365$) involved persons with a history of opioid overdoses, compared to non-fatal overdoses (68.55%, $n = 9979$).

Regarding census block group and census tract characteristics, fatal overdoses occurred in less populous block groups ($\bar{x} = 1361.04$) than non-fatal overdoses ($\bar{x} = 1411.10$), but fatal ($\bar{x} = 4259.96$) and non-fatal overdoses ($\bar{x} = 4281.88$) occurred in similarly sized census tracts. Fatal and non-fatal overdoses occurred in block groups and census tracts with comparable levels of racial/ethnic heterogeneity. Fatal overdoses disproportionately occurred in more residentially unstable block groups ($\bar{x} = 0.20$) and census tracts ($\bar{x} = 0.18$) than non-fatal overdoses ($\bar{x} = 0.16$ for block groups; $\bar{x} = 0.12$ for tracts). Fatal overdoses occurred in less disadvantaged block groups ($\bar{x} = 0.10$) and tracts ($\bar{x} = 0.12$) than non-fatal overdoses ($\bar{x} = 0.19$ for block groups; $\bar{x} = 0.22$ for tracts). Fatal overdoses occurred in block groups ($\bar{x} = 65.15$) and tracts ($\bar{x} = 157.81$)

Table 2
Event, person, census block group, and census tract characteristics of fatal and non-fatal opioid overdoses in boston, 2014–2019.

Variable	Fatal Overdoses (*N* = 1354)			Non-fatal Overdoses (*N* = 14,557)		
	Mean/N	(SD)/%	[Range]	Mean/N	(SD)/%	[Range]
Event Characteristics						
Hospital***	368	27.18		193	1.33	
Narcan***[a]	143	10.56		7814	53.68	
Person Age at Time of OD***[b]						
Under 30	248	18.32		3346	22.99	
30-39	392	28.95		4937	33.91	
40-49	310	22.90		2922	20.07	
Over 50	438	32.35		3606	24.77	
Year***[c]						
2014	98	7.24		1501	10.31	
2015	233	17.21		1959	13.46	
2016	257	18.98		2278	15.65	
2017	276	20.38		2764	18.99	
2018	244	18.02		2903	19.94	
2019	246	18.17		3152	21.65	
Person Variables						
Male	1012	74.74		10,613	72.91	
Race/Ethnicity						
White	873	64.48		9197	63.18	
African American	174	12.85		1801	12.37	
Hispanic	268	19.79		2897	19.90	
Other	39	2.88		662	4.55	
Previous Opioid ODs***	365	26.96		9979	68.55	
Block Group Factors						
Population***	1361.04	666.82	26-3987	1411.10	625.97	26-3987
Racial/Ethnic Heterogeneity	.52	.16	0–.79	.54	.16	0–.79
Residential Instability*	.20	.92	−2.30-3.42	.16	.85	−2.48-3.42
Concentrated Disadvantage**	.10	1.00	−1.87-3.53	.19	1.01	−1.87-4.52
Drug Crime Arrests***	65.15	176.15	0-1073	179.88	323.14	0-1073
Tract Characteristics						
Population	4259.96	1524.05	26-8961	4281.88	1600.12	26-8961
Racial/Ethnic Heterogeneity	.57	.14	.09–.75	.57	.14	.04–.75
Residential Instability**	.18	.90	−2.54-2.59	.12	.72	−2.54-2.59
Concentrated Disadvantage***	.12	.95	−1.39-3.06	.22	.94	−1.39-4.65
Drug Crime Arrests***	157.81	283.74	2-1854	354.49	521.93	0-1854

Abbreviations: SD = standard deviation.
*$p < .05$, **$p < .01$, ***$p < .001$, two-tailed tests for statistically significant difference between fatal and non-fatal overdoses.
[a] Includes 876 fatal and 2 non-fatal overdoses with missing Narcan information.
[b] Includes 1 fatal and 83 non-fatal overdoses with missing age information.
[c] Information for fatal opioid overdoses in 2014 is inconsistent with the other years in the study. The recording practices used throughout 2015–2019 were only implemented in August 2014, meaning that reliably recorded data is only available for September to December 2014.

with significantly less drug crime arrests than non-fatal overdoses ($\overline{x} = 179.88$ for block groups; $\overline{x} = 354.49$ for tracts).

3.3. *Predicting the odds of fatal opioid overdose relative to non-fatal opioid overdose*

The unconditional three-level logistic hierarchical and cross-classified random effects regression model without study covariates examines how variation in the outcome is apportioned among events, persons, block groups, and tracts. The unconditional model yielded variance component estimates of the person-level (0.41), block group-level (0.66), and tract-level (0.21) intercepts, indicating that approximately 72.1%, 9.0%, 14.4%, and 4.6% of the reliable variation in fatal opioid overdoses relative to non-fatal opioid overdoses was apportioned between events, persons, block groups, and tracts, respectively. Note that the level-one, event-level, intercept is held constant at $\frac{\pi^2}{3}$ in the model with logistic outcome (Snijders and Bosker, 1999).

Table 3 provides an examination of the event-, person-, block group-, and tract-level factors that predict the odds of a fatal opioid overdose relative to a non-fatal opioid overdose. The table presents odds ratios and 95% confidence intervals from a series of three-level logistic hierarchical and cross-classified random effects regression models.

Model 1 includes the event-level characteristics. Opioid overdose events in which Narcan was used were 66% less likely to end in a fatality (OR = 0.34, 95% CI = 0.28,.42). Additionally, opioid overdoses involving persons under the age of 30 were 24% less likely to end in a fatality than overdoses involving persons over 50 years (OR = 0.76, 95% CI = 0.57,1.01).

Model 2 includes the person-level variables. Males (OR = 1.14, 95% CI = 0.99,1.33) and African American individuals (OR = 1.39, 95% CI = 1.13,1.71) were significantly more likely to die during an opioid overdose event, relative to females and white individuals. Additionally, individuals with a history of opioid overdose were 80% less likely to die in a subsequent opioid overdose event (OR = 0.20, 95% CI = 0.18,.23).

Models 3 and 4 include block group and tract factors, respectively. Model 3 indicates that opioid overdoses occurring in block groups with lower levels of racial/ethnic heterogeneity (OR = 1.77, 95% CI = 0.90,3.50), and more drug crime arrests (OR = 0.92, 95% CI = 0.90,.95) were significantly less likely to result in fatalities. Similarly, Model 4 indicates that opioid overdoses occurring in census tracts with more drug crime arrests (OR = 0.96, 95% CI = 0.94,.97) were less likely to result in fatalities.

Table 3
Predicting fatal opioid overdoses (unity) versus non-fatal opioid overdoses (zero), $N = 15{,}911$ opioid overdose events, 8679 persons, 544 census block groups, 173 census tracts.

Variable	Model 1		Model 2		Model 3		Model 4		Model 5	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Event Characteristics										
Hospital	.32	[.07, 1.50]							.28	[.06, 1.26]
Narcan[a]	.34***	[.28, .42]							.31***	[.26, .38]
Person Age at Time of OD[b]										
Under 30	.76[a]	[.57, 1.01]							.75[a]	[.57, 1.00]
30-39	.84	[.65, 1.08]							.89	[.69, 1.14]
40-49	.91	[.69, 1.21]							.98	[.74, 1.30]
Year[c]										
2014	1.07[a]	[.75, 1.54]							1.07	[.75, 1.54]
2015	1.35	[.97, 1.86]							1.37[a]	[.99, 1.90]
2016	1.16	[.84, 1.61]							1.21	[.88, 1.68]
2017	1.18	[.87, 1.61]							1.27	[.94, 1.73]
2018	1.25	[.92, 1.70]							1.32[a]	[.98, 1.79]
Person Variables										
Male			1.14[a]	[.99, 1.33]					1.12	[.90, 1.39]
Race/Ethnicity[d]										
African American			1.39**	[1.13, 1.71]					.94	[.68, 1.31]
Hispanic			.94	[.80, 1.12]					.78	[.60, 1.01]
Previous Opioid ODs			.20***	[.18, .23]					.30***	[.25, .37]
Block Group Factors										
Population					1.01	[1.00, 1.03]			1.01	[1.00, 1.03]
Racial/Ethnic Heterogeneity					1.77[a]	[.90, 3.50]			2.08	[.72, 6.01]
Residential Instability					.94	[.83, 1.06]			.92	[.77, 1.10]
Concentrated Disadvantage					.93	[.82, 1.04]			.97	[.80, 1.16]
Drug Crime Arrests					.92***	[.90, .95]			.95**	[.93, .99]
Tract Characteristics										
Population							1.01	[1.00, 1.01]	1.00	[.99, 1.01]
Racial/Ethnic Heterogeneity							1.67	[.72, 3.88]	.62	[.18, 2.19]
Residential Instability							.94	[.83, 1.08]	.92	[.76, 1.11]
Concentrated Disadvantage							.97	[.84, 1.13]	1.00	[.80, 1.26]
Drug Crime Arrests							.96***	[.94, .97]	.98	[.96, 1.01]
Variance Components[e]										
Persons, b_{00j}	.36		.12		.39		.40		.12	
Block groups, c_{00kl}	.22		.62		.61		.68		.17	
Tracts, d_{00l}	.28		.16		.10		.08		.06	

Abbreviations: OR = odds ratio; CI = confidence interval.
Notes: A one unit change in block group and tract populations represents 100 persons.
[a] Models include variable representing missing Narcan.
[b] Reference = 50 and older; models include variable representing missing age.
[c] Reference = 2019.
[d] Reference = white; models include variable representing "other" and "missing" race/ethnicity.
[e] The table displays variance component estimates of the person (b_{00j}), census block group (c_{00kl}), and census tract (d_{00l}) level intercepts. The level 1 (event) variance is assumed to have a standard logistic distribution with constant variance, $\frac{\pi^2}{3}$. The unconditional models without study covariates produced variance component estimates of .41, .66, and .21 for persons, block groups, and tracts, respectively.$p < .05$ (one-tailed test); *$p < .05$, **$p < .01$, ***$p < .001$ (two-tailed tests).

Model 5 includes the results from the full model accounting for event-, person-, block group-, and tract-level characteristics simultaneously. The results for the event- and person-level factors are largely consistent with those presented in Models 1 and 2. Opioid overdoses were less likely to result in a fatality when Narcan was used, when the overdose victim was younger, and for individuals with history of opioid overdose. Conversely, the effects of gender and race/ethnicity were no longer statistically significant when the full array of covariates were accounted for. Regarding the block group and tract characteristics, only drug crime arrests remained significant in Model 5: a higher concentration of illicit drug activity in census block groups was associated with diminished odds of a lethal overdose.

Note that inclusion of the study covariates explained much of the person, census block group, and census tract variation in fatal versus non-fatal opioid overdoses observed in the unconditional model. The person-level variance component was reduced from .41 in the unconditional model to 0.12 in the full model, indicating that the inclusion of the study covariates explained 70.73% of the reliable variation in fatal versus non-fatal opioid overdoses at the person-level [$\frac{.41-.12}{.41}$]. The block group-level variance component was reduced from 0.66 in the unconditional model to 0.17 in the full model, indicating that the inclusion of the study covariates explained 74.24% of the reliable variation in fatal versus non-fatal opioid overdoses at the block group-level. The tract-level variance component was reduced from .21 in the unconditional model to 0.06 in the full model, indicating that the inclusion of the study covariates explained 71.43% of the reliable variation in fatal versus non-fatal opioid overdoses at the tract-level.

3.4. Sensitivity analysis

We estimated a series of supplemental statistical models to examine the robustness of the study findings. First, we recognize Table 2 fallacy problem, or the mistaken interpretation of multiple adjusted effect estimates from a single model in a single table (Westreich and Greenland, 2013). To protect against this potential problem, we estimated multiple models at different levels of analysis (see Table 3), as well as multiple models with different covariate subsets, both within and between levels of analysis. The multiple models indicated that the coefficients presented in Table 3 were robust to Table 2 fallacy problem, providing confidence in the findings.

Second, an appreciable number of opioid events occurred in or near hospital grounds or had missing Narcan information. In both instances, these events were disproportionately concentrated among fatal opioid overdoses. While the statistical models included appropriate controls to account for these features of the opioid events, models were re-estimated after excluding: (1) opioid overdose events that occurred in or near hospital grounds; and (2) events with missing Narcan information. The results, presented in Appendix B, were substantively unchanged, lending credence to the study findings.

Third, it is possible that Boston Police Department drug crime arrests were influenced by extralegal factors such as resident race and ethnicity. To assuage this concern, the analysis included a measure of racial/ethnic heterogeneity (see Table 3). In supplemental models, we also estimated models controlling for the percent of the population black (*ns*) and percent of the population Hispanic (*ns*). The results were substantively unchanged using this approach.

4. Discussion

This study employed descriptive, spatial, and multilevel regression techniques to examine the salience of contextual characteristics for fatal and non-fatal opioid overdoses in Boston from 2014 to 2019. The first aim of this study was to examine the contextual correlates of block group counts of (fatal and non-fatal) opioid overdose. Longitudinal negative binomial models with random effects indicated that higher levels of concentrated disadvantage, residential instability, and illicit drug activity were associated with higher annual block group counts of total opioid overdoses. These findings support the growing evidence that the opioid epidemic crisis is partially rooted in contextual characteristics (Yuchen et al., 2022). Recent studies utilizing both spatial (Hollingsworth et al., 2017; Pear et al., 2019) and multilevel (Altekruse et al., 2020; Flores et al., 2020; Galea at el., 2003) regression techniques have substantiated an array of areal social and economic characteristics (e.g., socioeconomic disadvantage, residential instability, educational attainment, and safety) as important predictors of opioid overdoses, particularly fatal opioid overdoses. Ultimately, predictive models incorporating community-level predictors are critical for optimizing public health resource allocation and designing effective community-based interventions. For example, a consideration of community factors could help policy-makers: (1) anticipate the types of areas with high rates of opioid overdose and opioid overdose mortality; and (2) determine where to allocate resources—such as naloxone distribution, street outreach, and investment dollars—for community-based opioid prevention interventions (Schell et al., 2022, pp. 530–531).

The second aim of the study was to examine the event, person, census block group, and census tract characteristics that distinguished fatal and non-fatal opioid overdose. A series of *t*-tests and Chi-square tests for categorical data provided a descriptive comparison of the independent variables across fatal and non-fatal opioid overdoses. Logistic hierarchical and cross-classified random effects models predicted the odds of fatal opioid overdose relative to non-fatal opioid overdose with relevant event, person, census block group, and census tract factors. Together, the results from these analyses indicated that event- and person-level factors distinguished fatal and non-fatal opioid overdose. In fact, the unconditional multilevel model demonstrated that more than 80% of the reliable variation in fatal opioid overdose relative to non-fatal opioid overdose was attributed to event- and person-level factors.

The use of Narcan in an opioid overdose event was particularly salient, reducing the odds of a fatality by almost 70%. This finding corresponds with prior research demonstrating the effectiveness of opioid antagonists as an antidote to opioid overdose (Davis and Carr, 2019). Increasing the prevalence of Narcan and other medications for opioid use disorder (such as Buprenorphine) at the street level is a simple and direct pathway toward reducing deaths resulting from opioid overdose, primarily due to their ease of use (Smart and Davis, 2021). While every state in the U.S. currently has some form of a naloxone access law, not every state has a prescription that allows anyone to access naloxone. Specific aspects of the state legislation vary, but these laws generally aim to facilitate easier access to naloxone, or an opioid antagonist, through expanding the capabilities of prescribers. According to the Stop the Addition Fatality Epidemic (SAFE) Project, 48 states and Washington D.C. have “third party” laws that permit prescribers to issue an opioid antagonist prescription to someone who is not the intended user. Additionally, 47 states and Washington D.C. have “standing orders” that grant a healthcare provider the ability to prescribe an opioid antagonist to a group of people rather than requiring individual prescriptions (SAFEProject, 2022).

In Massachusetts, the first iteration of a naloxone access law was implemented in 2014 via a standing order that mandated naloxone be carried by first responders in the course of their duties (MacQuarrie, 2014). Codified into law by M.G.L. c. 94C, § 19B, Massachusetts has a standing order that permits any licensed pharmacist in the Commonwealth to dispense an opioid antagonist to persons at-risk of experiencing an overdose and those who may encounter an overdose victim (The 192nd General Court of the Commonwealth of Massachusetts, 2022). Evidence suggests that this standing order has increased access to naloxone. The most recent available data indicate that the number of naloxone dispensing events in pharmacies under the standing order increased from 1679 in 2015 to 5624 in 2017 (Chatterjee et al., 2022). Pollini et al. (2020) assessed the accessibility of naloxone at pharmacies under the Commonwealth’s standing order. The study involved two attempts to purchase naloxone at approximately 200 randomly sampled retail pharmacies from May 2018 to April 2019: one attempt by a user of illicit opioids; and another attempt by someone who had a relationship with an illicit opioid user. Of the 397 purchase attempts, 81.1% were successful with no significant differences between user and bystander attempts (Pollini et al., 2020).

Ultimately, the prevalence of opioid antagonists at the street level in Massachusetts provides a pathway toward reducing opioid overdose fatalities. Similarly, increased access to opioid antagonists has been hailed as a success in France, where overdose rates are among the lowest in Europe (Nguemeni Tiako et al., 2022). Similarly, research by Rowe et al. (2016) in San Francisco suggests that locating Narcan distribution sites in areas with high levels of overdose risk encourages opioid overdose reversals. And, a Narcan distribution program called Bmore POWER (Peers Offering Wellness Education and Resources) in Baltimore City, Maryland has also shown signs of success. Bmore POWER aims to create a sense of community responsibility around overdose prevention by recruiting residents with recent or current lived experience with drug use to conduct outreach in high-opioid-overdose-risk neighborhoods. This peer- and street-based based approach can “facilitate access to services among stigmatized and marginalized communities that distrust traditional providers, and benefit both the peer and the community members with whom they interact” (Owczarzak et al., 2020, p. 2).

In states where opioid antagonists are less readily available at the street level, however, access to opioid antagonists relies on: bystander reporting of opioid overdoses; time to response by emergency medical services; and the deployment of public health teams to areas of intense drug use and drug crime. Bystander reporting of opioid overdoses has decreased since the onset of COVID-19, which has exacerbated heightened periods of isolation and solitary opioid use (Lippold et al., 2019). But, the average time for emergency medical services to reach someone who experienced an opioid overdose event in 2022 was under 10 min, according to the White House's Office of National Drug Control Policy (ONDCP) Non-Fatal Opioid Overdose Tracker (NEMSIS, 2022). Additionally, concentrating public health teams in areas of high intensity drug crime is a cornerstone of the Overdose Response Strategy (ORS), a collaborative effort between the Centers for Disease Control and Prevention (CDC) and the High Intensity Drug Trafficking Areas (HIDTA) program (CDC, 2022b).

The results also indicated that the odds of fatal opioid overdose relative to non-fatal opioid overdose were reduced by 70% for individuals who had a history of (non-fatal) opioid overdose. This finding is seemingly at odds with research demonstrating that fatal opioid overdoses are often preceded by non-fatal overdoses (Caudarella et al., 2016; Olfson et al., 2018). Rather, this finding suggests that individuals with a history of (non-fatal) opioid overdose are protected in a manner that individuals who overdose for the first time are not. Considering potential explanations for this, prior research has indicated that individuals who experience a non-fatal overdose may become more cautious regarding future drug use, serving to reduce their risk of a fatal overdose (Mathers et al., 2013). It is also possible that individuals with a history of opioid overdose are less likely to use opioids in isolation. Accordingly, research suggests that the social networks of individuals who use opioids can reduce the risk of fatal overdose, either through the provision of antidotes such as Narcan (Latkin et al., 2019; Smart and Davis, 2021) or simply by being present and capable of intervening in the event of an overdose (Caudarella et al., 2016). However, it should be noted that the relationships between individuals within such social networks are complex and the decision to intervene in an overdose is dependent on various factors, including the fear of legal consequences if authorities become involved (Bowles et al., 2020; Rouhani et al., 2021; Wygonik et al., 2021).

The descriptive and multilevel analyses also indicated that the social context distinguished fatal and non-fatal opioid overdose. In fact, the unconditional multilevel model indicated that an appreciable proportion of the reliable variation in fatal opioid overdose relative to non-fatal opioid overdose—20%—was attributed to census block groups and census tracts. Most notably, the odds that an overdose resulted in a fatality decreased by 4% for every ten drug crime arrests in the proximal (census block group) environment and 2% for every ten drug crime arrests in the distal (census tract) context. As drug-related arrests are viewed as a meaningful indicator of drug-use trends (Rosenfeld and Decker, 1999), this finding may be explained by the disproportionate concentration of public health services in areas with high levels of drug crime in Boston, which translates to increased and faster opportunities for intervention during an opioid overdose event. For instance, the City of Boston deploys a Coordinated Response Team—constituted by the BPHC, the Boston Police Department (BPD), street outreach workers, and others—that provides Narcan, counseling, and related services to individuals suffering from opioid use disorder in areas of intense drug use and drug crime, such as the intersection of Massachusetts Avenue and Melnea Cass Boulevard. It is also possible that overlap in drug-using and drug-selling spaces (Hunter et al., 2018) suggests the presence of a subculture whereby strategies are shared to mitigate risks that accompany regular drug use (Rouhani et al., 2021; Wygonik et al., 2021). Indeed, opioid use in areas with more drug use and drug crime can mitigate fatal overdose via immediacy to other drug users who are capable of intervening in an overdose (Caudarella et al., 2016), including via the administration of antidotes such as Narcan (Latkin et al., 2019; Smart and Davis, 2021). Similarly, studies have demonstrated that areas with high levels of drug use are in close proximity to hospitals (Chen et al., 2022), health centers (Flores et al., 2020), and treatment centers (Chichester et al., 2020) that can intervene and protect against mortality during an opioid overdose event.

While the findings of this analysis indicate that the social context had a direct impact on the odds of fatal opioid overdose relative to non-fatal opioid overdose, it is also noteworthy that the social context impacted the odds of fatal versus non-fatal opioid overdose indirectly. The results from a person-specific model indicated that African American individuals were 39% more likely than white individuals to die during an opioid overdose. Historically, African Americans have been associated with lower opioid fatality rates than whites (Shiels et al., 2018; Shipton et al., 2018), but recent research indicates that both fatal and non-fatal opioid overdoses have increased sharply among African Americans, while decreasing among non-Hispanic whites (Friedman et al., 2021; Furr-Holden et al., 2021; Hedegaard et al., 2021a; Khatri et al., 2021; Ochalek et al., 2020). For example, examining county-level overdose death rates in Ohio from 2007 to 2018, Kline et al. (2021) demonstrated that overdose death rates were higher for white residents than for black residents early in the study period. However, in many counties, overdose death rates for black residents increased throughout the study period and were comparable to overdose death rates for white residents by the end of the study. Similarly, Ghose et al. (2022) demonstrated that the COVID-19 pandemic significantly increased opioid overdose deaths in Milwaukee County, Wisconsin, but the more pronounced effects were observed in poor, urban neighborhoods disproportionately impacting black and Hispanic communities. This research coincides with a documented shift in opioid overdoses from rural areas with majority white populations (Hedegaard et al., 2021b; Shipton et al., 2018) in the 2000s and early 2010s, to urban areas with more racially diverse populations in the middle and late 2010s (Hedegaard et al., 2021b; Lippold et al., 2019; Rodda et al., 2020).

In this study, however, the effects of race/ethnicity were rendered insignificant after the census block group and census tract characteristics were accounted for. Interestingly, opioid overdose events involving African American individuals were concentrated in block groups with significantly less drug crime arrests (150) than opioid overdose events involving white individuals (174). If the assertions above are correct, and public health services that translate to increased and faster opportunities for intervention during an opioid overdose event are disproportionately concentrated in areas where drug activity is more rampant, then environmental factors could be a key to understanding racial and ethnic differences in opioid overdose fatalities and interventions. Existing research has already demonstrated the importance of social and economic factors (such as housing status and type of health insurance) for understanding racial and ethnic disparities in relation to access to medications for opioid use disorder (Goedel et al., 2020; Kalmin et al., 2021).

More broadly, the results support the premise that opioid use, and individual behavior more broadly, is influenced by the social context. For example, Bronfenbrenner's (1979) bio-ecological model of human development conceptualizes social behavior as deriving from factors in multiple, nested social contexts, including immediate environments (e.g., neighborhoods) and indirect environments (e.g., economic, educational, and political systems). Drawing on Bronfenbrenner's (1979) research, Jalali et al. (2020) formulated a social-ecological framework of opioid misuse that situates opioid use disorder in individual (e.g., socio-demographic factors, stress and trauma exposure, biological and genetic susceptibility), interpersonal (e.g., family history of substance abuse, influence of family and friends), community (e.g., access to legal and illegal opioids, community norms, workplace and school factors), and societal (e.g., law enforcement and policing, government programs and regulations, economic conditions) factors. This framework recognizes the multidimensional complexity of opioid use—and in particular, the importance of social context. Consistent with the Jalali et al.'s (2020) social-ecological framework, our findings indicated that drug crime arrests in the broader social context—at the block group level and the census tract level—were associated with opioid overdoses. Ultimately, the findings support multilevel theorizing, such as the social-ecological framework, and multilevel analysis as mechanisms to more fully understand the multi-faceted causes of opioid overdose.

Several data constraints temper the study findings and conclusions. First, the Commonwealth of Massachusetts VRS provided data on all fatal opioid overdoses between August 30, 2014, and December 31, 2019. Because VRS data were unavailable prior to August 30, 2014, BPHC data were used to identify overdose fatalities during this time period. Yet, these estimates were conservative because: (1) BPHC data were limited to overdoses that resulted in an emergency call to EMS; and (2) EMS data were not updated beyond the initial response (e.g., if the victim later died).

Second, the combined Boston EMS and Massachusetts VRS data identified 17,725 opioid overdoses in Boston from January 2014 to December 2019, but the study sample was restricted to 15,911 fatal and non-fatal opioid overdoses that: had valid geographic identifiers; did not occur in empty (zero population) census-designated block groups or tracts; did not involve multiple persons; and did not have missing unit-level person information. An analysis of attrition indicated that the excluded cases were not substantively different than the included cases, but we cannot ensure that the data were missing completely at random.

Third, we partitioned the variance by holding the level one variance term constant at $\frac{\pi^2}{3}$, the conventional approach for logistic, probit, and other generalized linear models (Hox, 2010; Snijders and Bosker, 1999). Yet, we acknowledge that calculating the intraclass correlation coefficient incorrectly can lead to misleading conclusions about the relative contribution of opioid overdose factors at each level of analysis. Accordingly, some literature contends that the latent variable approach used in this study is only appropriate when the response variable can be conceptualized as the discretization of an underlying continuous latent variable (Goldstein et al., 2002). Additional research has proposed different methods for calculating the intraclass correlation coefficient, indicating that ICC estimates can differ across methods, although confidence intervals typically overlap (Wu et al., 2012).

Finally, the odds ratio as a measure of the strength of association between an independent variable and outcome approximates relative risk when the outcome is rare (less than 10%). However, as the frequency of the outcome increases, the odds ratio will overestimate relative risk when it is more than one and underestimate relative risk when it is less than one (Davies et al., 1998; Zhang and Yu, 1998). The frequency of fatal opioid overdose in the study sample was 8.51% ($N = 1354$). As such, we do not anticipate the associations presented in Table 3 to be underestimated or overestimated. Nonetheless, we recognize the possibility that fatal opioid overdose (relative to non-fatal opioid overdose) exceeds 10% in the population, which could lead to underestimated or overestimated effect sizes.

5. Conclusions

With these limitations in mind, the findings affirm two key insights for future research and policy. First, the findings indicated that fatal and non-fatal opioid overdoses have distinct etiologies. As such, research focused solely on fatal overdoses could potentially miss evolving patterns in non-fatal opioid overdoses that subsequently lead to more deaths. To date, there have been few studies focused on examining changes in non-fatal opioid overdoses, all of which have reported increased rates in non-fatal overdose-related Emergency Department visits (as a proportion of all ED visits) during 2020 compared with previous years (Ochalek et al., 2020; Rodda et al., 2020; Soares et al., 2022).

Second, the findings affirm the importance of social context in research on opioid overdose. Theoretically, this premise recognizes that individuals are shaped by: the spaces and places in which they live and act; and their relationships with persons, law enforcement, socio-political economies, and informal codes of conduct in these spaces and places (Ivsins et al., 2019). Consistent with Jalali et al.'s social-ecological framework of the opioid crisis, our findings suggest that aspects of both the communal and societal environment are relevant to opioid use. We therefore cannot disentangle opioid overdose events from the broader social contexts in which they occur. Practically, public-health officials should recognize that interventions intended to reduce opioid overdose deaths need to be tailored to the environmental context, which requires understanding the factors that contribute to regional variation in opioid overdoses (Lippold et al., 2019; Nguemeni Tiako et al., 2022). Only through the consideration of the social context can we optimize the allocation of public health resources and targeted interventions to reduce fatal and non-fatal opioid overdoses (Schell et al., 2022).

Data availability

The data that has been used is confidential. This project was funded by Arnold Ventures. We thank Ben Struhl and Andrew Papachristos for their support when writing the manuscript and Boston City Hall, Boston Public Health Commission, Boston Emergency Medical Services, and the Boston Police Department for their support in data collection.

Appendix A

Equations 1–5 provide the formulas for the unconditional three-level logistic hierarchical and cross-classified random effects model without study covariates. In equation (1), the model uses the binomial sampling distribution and logit link function for dichotomous outcomes. Note that the logit link function provides a mathematical transformation allowing the dichotomous dependent variable to function as a linear prediction of the independent variables in the model:

$$\text{Logit Link}\eta\_(ijkl) = \ln\left[\frac{p}{1-p}\right] = \ln\left[\frac{p(\text{Fatal Overdose})}{1-p(\text{Fatal Overdose})}\right] = \ln\left[\frac{p(\text{Fatal Overdose})}{p(\text{Non}-\text{fatal Overdose})}\right] \tag{1}$$

$$\text{Level 1 } \eta_{ijkl} = \pi_{0jkl} \tag{2}$$

$$\text{Level 2 } \pi_{0jkl} = \theta_{0l} + b_{00j} + c_{00kl} \tag{3}$$

$$\text{Level 3 } \theta_{0l} = \delta_{000} + d_{00l} \tag{4}$$

$$\text{Full Model } \eta_{ijk} = \delta_{000} + b_{00j} + c_{00kl} + d_{00l} \tag{5}$$

In equation (1), p represents the probability of a fatal opioid overdose and $1 - p$ represents the probability of a non-fatal overdose. The term $\frac{p}{1-p}$ represents the odds of a fatal opioid overdose *relative to* a non-fatal opioid overdose, and taking the natural log (ln) of $\frac{p}{1-p}$ provides the log odds of a fatal opioid overdose relative to a non-fatal opioid overdose. The dependent variable, η_{ijkl}, is thus the log-odds of a fatal opioid overdose relative to a non-fatal opioid overdose for event *i* cross-classified in person *j* and census block group *k*, nested within census tract *l*.

In the level-1 (event-level) model (equation (2)), η_{ijkl} is estimated by the overall intercept, π_{0jkl}, as the mean likelihood that a fatal opioid overdose occurs relative to a non-fatal opioid overdose within persons, *j*, census block groups, *k*, and census tracts, *l*. There is no level-one variance component included in the logistic hierarchical and cross-classified random effects regression model because it is determined by *p* and therefore unidentified; the level 1 error term is assumed to have a standard logistic distribution with constant variance, $\frac{\pi^2}{3}$ (Snijders and Bosker, 1999).

At level-two (equation (3)), the overall intercept, π_{0jkl}, is modeled as a function of the level-two intercept, θ_{0l}, the random person-level term, b_{00j}, and the random block group-level term, c_{00kl}. At level-three (tract-level) in the model (equation (4)), θ_{0l} is modeled as a function of the grand mean intercept, γ_{000}, and the random tract-level effect, d_{00l}. The full unconditional model (equation (5)) decomposes the total variance into four terms: an event-level variance term, $\frac{\pi^2}{3}$, for grand-mean intercept, γ_{000}; a person-level variance, b_{00j}; a block group-level variance, c_{00kl}, and a tract-level variance, d_{00l}. This model examines the proportion of total variance that is attributable to event-level differences within persons, block groups, and tracts, as well as between-person, between-block group, and between-tract differences.

The random intercept model in equations 6–8 adds predictor variables to the unconditional model, allowing the intercept to take on different values for each event, person, census block group, and census tract in the data. Expanded to include the relevant event-level, person-level, block group-level, and tract-level factors, the random intercept model becomes:

$$\text{Level 1 } \eta_{ijkl} = \pi_{0jkl} + \pi_{1jkl}Hospital_{ijkl} + \pi_{2jkl}Narcan_{ijkl} + \pi_{3jkl}AgeUnder30_{ijkl} + \pi_{4jkl}Age30\text{-}39_{ijkl} + \pi_{5jkl}Age40\text{-}49_{ijkl} + \pi_{6jkl}Year2014_{ijkl} + \pi_{7jkl}Year2015_{ijkl} + \pi_{8jkl}Year2016_{ijkl} + \pi_{9jkl}Year2017_{ijkl} + \pi_{10jkl}Year2018_{ijkl} \tag{6}$$

$$\text{Level 2 } \pi_{0jkl} = \theta_{0l} + \gamma_{011}Male_j + \gamma_{012}AfricanAmerican_j + \gamma_{013}Hispanic_j + \gamma_{014}PreviousOpioidOD_j + \beta_{011}Population_{kl} + \beta_{012}Heterogeneity_{kl} + \beta_{013}Instability_{kl} + \beta_{014}ConcentratedDisadvantage_{kl} + \beta_{015}DrugArrests_{kl} + b_{00j} + c_{00kl} \tag{7}$$

$$\text{Level 3 } \theta_{0l} = \delta_{000} + \delta_{001}Population_l + \delta_{002}Heterogeneity_l + \delta_{003}Instability_l + \delta_{004}ConcentratedDisadvantage_l + \delta_{005}DrugArrests_l + d_{00l} \tag{8}$$

The level-one model (equation (6)) includes: whether or not the overdose event occurred on hospital property; whether or not Narcan was used during the event; and several dummy variables indicating person age at the time of event (reference = over 50). These factors are modeled as fixed effects via coefficients π_{1jkl} through π_{5jkl}. The focus of the level-one model is to estimate the event-level effects while controlling for statistical dependence within persons and census units. Additionally, because the data is a pooled, cross-sectional time series, we include 5 dummy variables representing each cross-section from 2014 to 2019 minus one, *Year2014* through *Year2018*. These factors are modeled as fixed effects via coefficients π_{6jkl} through π_{10jkl}. Including these fixed effects in the model purges the regression model from cross-sectional bias by controlling for between-year differences within persons and census units, thereby pooling the substantive event-, person-, block group- and tract-level effects across the study time frame.

The level-two model (equation (7)) represents the cross-classified part of the model and includes person-level factors (male, African American, Hispanic, and previous opioid overdoses) as well as block group-level factors (population, racial/ethnic heterogeneity, residential instability, concentrated disadvantage, and drug crime arrests). The person-level factors are modeled as fixed effects via coefficients γ_{011} through γ_{014}. The block group factors are modeled as fixed effects through coefficients β_{011} through β_{015}. The focus of the level-two model is to estimate between-person and between-block group variation in person and block group means as a function of person-level and block group-level factors.

The level-three model (equation (8)) includes tract-level factors (population, racial/ethnic heterogeneity, residential instability, concentrated disadvantage, and drug crime arrests) modeled as fixed effects via coefficients δ_{001} through δ_{005}. The focus of the level-three model is to examine between-tract variation in the outcome. Taken together, equations 6–8 estimate the joint influence of the event-, person-, block group-, and tract-level factors.

Appendix B. Predicting Fatal Opioid Overdoses (Unity) versus Non-fatal Opioid Overdoses (Zero), Excluding Opioid Overdoses that Occurred in or Near Hospital Grounds or had Missing Narcan Information, *N* = 14,839 Opioid Overdose Events, 7894 Persons, 543 Census Block Groups, 173 Census Tracts

Variable	OR	95% CI
Event Characteristics		
Narcan	.31***	[.26, .38]
Person Age at Time of OD[a]		
Under 30	.75*	[.56, .99]
30-39	.90	[.70, 1.16]
40-49	.97	[.73, 1.28]
Year[b]		
2014	1.10	[.76, 1.57]
2015	1.37	[.99, 1.90]
2016	1.21	[.87, 1.68]
2017	1.26	[.92, 1.71]
2018	1.33	[.98, 1.81]
Person Variables		
Male	1.11	[.89, 1.38]
Race/Ethnicity[c]		
African American	.91	[.65, 1.27]
Hispanic	.78	[.60, 1.02]

(continued on next page)

(*continued*)

Variable	OR	95% CI
Previous Opioid ODs	.30***	[.25, .37]
Block Group Factors		
Population	1.01	[.99, 1.03]
Racial/Ethnic Heterogeneity	2.17	[.75, 6.32]
Residential Instability	.91	[.76, 1.09]
Concentrated Disadvantage	.96	[.80, 1.16]
Drug Crime Arrests	.96**	[.93, .99]
Tract Characteristics		
Population	1.00	[.99, 1.01]
Racial/Ethnic Heterogeneity	.60	[.17, 2.12]
Residential Instability	.91	[.75, 1.11]
Concentrated Disadvantage	1.03	[.82, 1.30]
Drug Crime Arrests	.98	[.96, 1.01]
Variance Components[d]		
Persons, b_{00j}	.05	
Block groups, c_{00kl}	.18	
Tracts, d_{00l}	.05	

Abbreviations: OR = odds ratio; CI = confidence interval.
Notes: A one unit change in block group and tract populations represents 100 persons.
[a]Reference = 50 and older; models include variable representing missing age.
[b]Reference = 2019.
[c]Reference = white; models include variable representing "other" and "missing" race/ethnicity.
[d]The table displays variance component estimates of the person (b_{00j}), census block group (c_{00kl}), and census tract (d_{00l}) level intercepts. The level 1 (event) variance is assumed to have a standard logistic distribution with constant variance, $\frac{\pi^2}{3}$. The unconditional models without study covariates produced variance component estimates of 0.36, 0.23, and 0.23 for persons, block groups, and tracts, respectively.
*$p < .05$, **$p < .01$, ***$p < .001$ (two-tailed tests).

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