Supplemental material

Urban scaling of opioid overdose deaths in the United States: a cross-sectional study in three periods between 2005 and 2017

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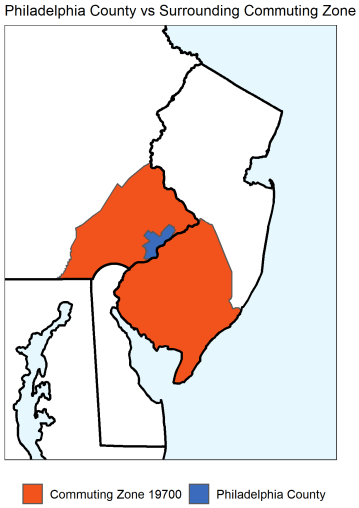
Section 1: description of Commuting Zones

Commuting zones: Commuting zones (CZs) are aggregations of counties based on commuting patterns (Tolbert and Sizer, 1996). We used the 1990 commuting zone delineation (https://www.ers.usda.gov/data-products/commuting-zones-and-labor-market-areas/). The 741 CZs cover the entirety of the U.S. providing a complete picture of the country, from rural to highly urbanized areas. Several CZs involve counties from more than one state. The map below shows an example of a CZ that involves the county of Philadelphia (blue) and the surrounding counties (in PA and NJ - orange) that share strong economic ties. These three counties form one CZ. The boundaries of the CZs are in perfect overlap with county boundaries.



The next map shows another example of CZ and county overlap. Below are the counties in the state of Pennsylvania and the CZs they belong to:

Section 2: Data imputation for records that had "unspecified drug" as contributory cause of death code

We imputed opioid involvement in records that had an unspecified drug code (T50.9) but did not have any other drug code. We did this in the following 7 steps:

1. We estimated period-specific probit models for the subset of records that had at least one drug specified.
2. We then created a dichotomous variable set to one if any opioid drug code was present and zero if no opioid codes were present.
    a. Opioid drug codes included T40.0, T40.1, T40.2, T40.3, T40.4, and T40.6. These records were coded as 1.
    b. Poisoning deaths not associated with opioids were coded as 0. These could be deaths associated with cocaine or other non-opioid drugs.
    c. Records with only unspecified drug code (T50.9) were set to missing.
3. We also created dichotomous variables for three major opioid groups, prescription opioids (T40.2), heroin (T40.1), and synthetic opioids other than methadone (T40.4).
    a. Each death certificate may include more than one contributory code thus one death can be classified in more than one group.
4. We then estimated models for all opioids and by opioid type (prescription, heroin and synthetic). Model predictors included:
    a. (1) Individual-level dichotomized variables (from death certificates) for sex, race/ethnicity (Hispanic, white non- Hispanic (ref), black non-Hispanic, others), marital status (married vs. not), education categories (< high school, high school graduate, some college, college or more), 10-year age categories (less than 30, 31-40, 41-50, 51-60, 61-70, 71-80, 81 and older), day-of-the week, and location of death (hospital inpatient, hospital outpatient/ED, dead on arrival, home and other).
    b. (2) County- level continuous variables for percent of the population below poverty, proportion of residents in the education categories previously mentioned, percent of household headed by females, median income, number of physicians per 1,000 people, log of population, and percent change in population.
    c. (3) State-level predictors for type of death investigation system (centralized medical examiner, decentralized medical examiner, coroner system and mixed), law requiring autopsy to be performed by pathologist (y/no) and a variable for US region (Northeast, Midwest, South and West).
5. Next, we estimated the predicted probability of the outcomes. We used the formula below:

$$P[Y_i = 1] = \Phi(X_i * \beta)$$

Where Y is the outcome (0/1) and X is a vector of predictors.

6. Finally, we assigned records with missing outcome to either 0 or 1 based on the predicted probability.
7. After assigning the records with unspecified codes to either 0 or 1 for the main outcome

(opioid overdose) and secondary outcomes (prescription opioid, heroin, and synthetic opioids), we calculated the total number of deaths for each of the outcomes in the CZs.

The data sources used are below:

a. County-level median income, poverty estimates, population, and education level: Census data. County-level Data Sets. https://www.ers.usda.gov/data-products/county- level-data-sets/

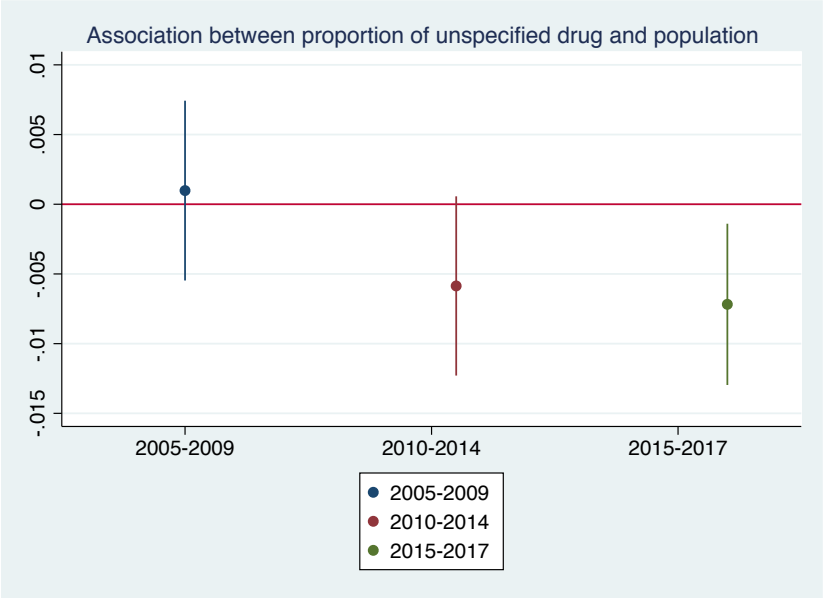
b. County-level percent of household headed by females and number of physicians: Area Health Resource Files. Health Resources and Services Administration. https://data.hrsa.gov/data/download

c. State-level predictors related to the death surveillance system: Centers of Disease Control and Prevention. https://www.cdc.gov/phlp/publications/coroner/death.html

Section 3

Supplemental Figure and Tables

Figure S1: Coefficients of association between proportion of unspecified drug code and population size in three periods



Note: These coefficients were obtained regressing the proportion deaths with unspecified codes among all drug poisoning codes and the log of population.

Table S1: Median percentage of overdose deaths with unspecified codes per Census Region in three periods

	2005-2009		2010-2014		2015-2017	
Region	Median	25th-75th	Median	25th-75th	Median	25th-75th
Northeast	18.9	6.3-39.2	9.6	2.7-34.2	3.2	1.3-28.9
Midwest	22.7	7.2-40	23.6	8.3-40.5	14.3	3-29.3
South	25	9.1-38.7	24.9	11.9-37.1	12.5	3.8-25
West	19.8	6.8-33.3	18.9	3.5-30.8	7.5	0-22.6

Table S2: Scaling coefficients from original data compared to imputed data in three periods.

		2005-2009	2010-2014	2015-2017
Imputed data	Scaling coefficient	1.11	1.11	1.16
	95% CI	1.07-1.14	1.08-1.14	1.13-1.20
Original data	Scaling coefficient	1.08	1.09	1.16
	95% CI	1.04-1.12	1.06-1.13	1.12-1.19

Table S3: Scaling coefficients including only 409 CZs that had at least one death involving each opioid type.

		2005-2009	2010-2014	2015-2017
Prescription opioid	Scaling coefficient	0.94	0.91	0.97
	95% CI	0.89-0.99	0.86-0.96	0.92-1.02
Heroin	Scaling coefficient	1.19	1.22	1.22
	95% CI	1.12-1.27	1.14-1.29	1.15-1.29
Synthetic opioid	Scaling coefficient	0.86	0.88	1.11
	95% CI	0.81-0.91	0.83-0.93	1.03-1.18