Community-level characteristics associated with Over-The-Counter Pharmacy Sale of Naloxone and Opioid-related Overdose Fatalities in Massachusetts

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5.11.2016

Introduction

Deaths from opioid-related overdoses have doubled in Massachusetts (MA) since 2012, with 1,379 statewide fatalities in 2015, up from about 600 annually between 2006-2012 [1]. The 2014 state-wide rate of 18.6 deaths per 100,000 was the highest ever for unintentional fatal opioid-related overdose. Of the 351 municipalities in MA, 221 (61%) had at least one overdose death in 2015. This parallels national trends: fatal heroin overdose has recently increased across multiple demographic groups [2]. Fentanyl, a more potent opioid than heroin, is implicated in this steep increase in fatal overdoses in both MA and nationally [3,4].

Community distribution of naloxone, an opioid reversal agent, to community members is known to reduce community-level deaths from overdose and is widely implemented across the US [5,6]. Increasingly, retail pharmacies over-the-counter naloxone sales are being utilized to increase the availability of naloxone to community members [7]. Two main methods for distributing naloxone are employed in MA: free distribution and training through the Massachusetts Department of Public Health (MDPH) Overdose Education and Naloxone Distribution (OEND) Program, and a standing order enabling individual purchase of naloxone at pharmacies statewide without a prescription.

Prior neighborhood-level spatial studies have found naloxone distribution in areas of concentrated opioid use and overdose risk is associated with increased overdose reversals in those areas, but gaps remain to support this spatial assessment in areas of less concentrated overdose risk [8]. This project assesses the availability of naloxone in MA through pharmacies participating in the standing order and the OEND program. Additionally, I analyzed associations between community-level fatal opioid overdose rate and community-level risk factors for opioid use and overdose [1,9].

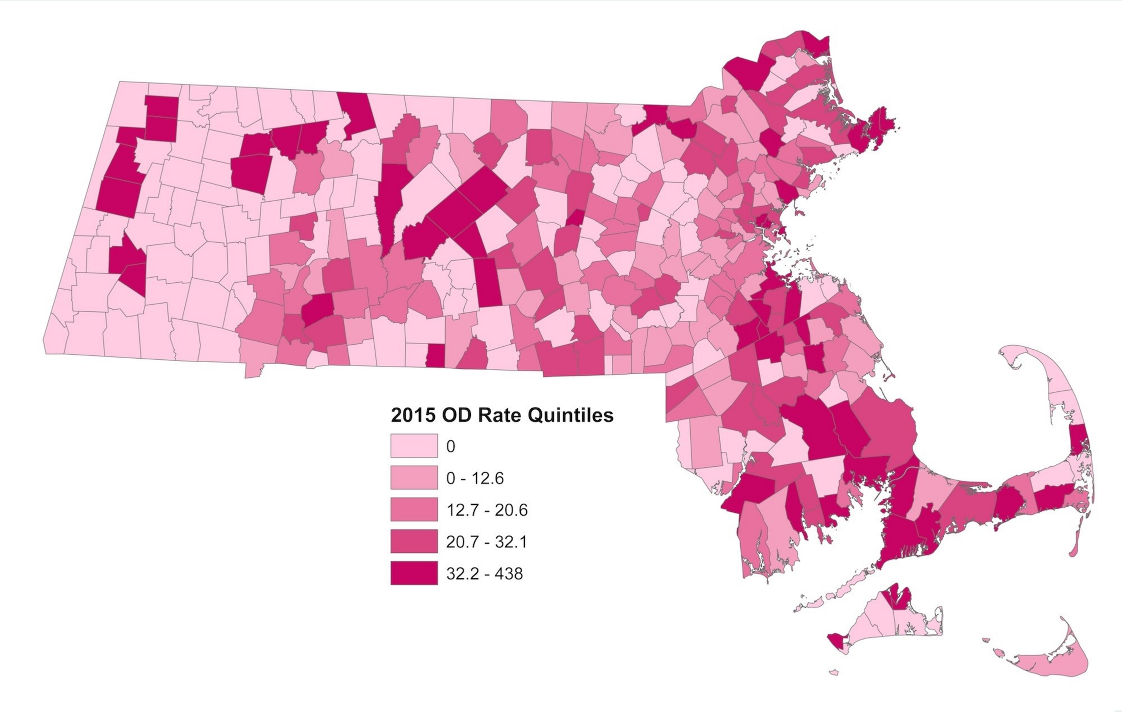

Figure 1. 2015 fatal opioid-related overdose rate by city/town. Displayed by Quintiles.

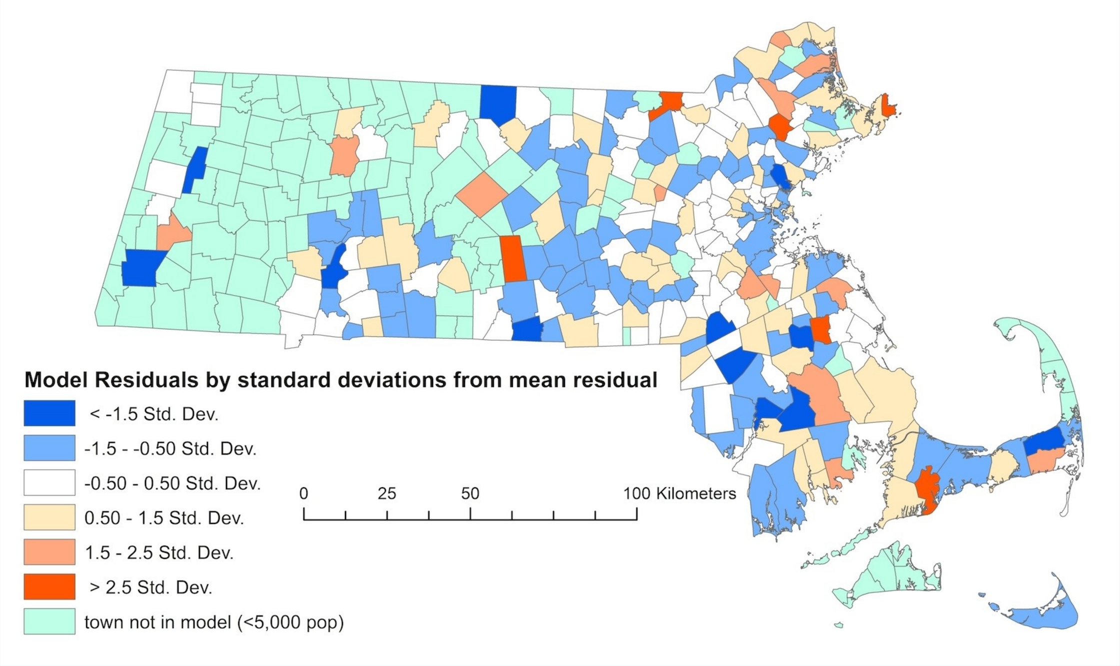

Figure 2. Linear regression model residuals plotted by city/town for communities with greater than 5,000 population. Residuals are plotted by standard deviation from mean residual. See Table 1 for list of communities with extreme values.

Methods

Linear Regression
Linear regression was conducted on all MA city/towns with population >5,000 (n=245). All data in the model were at the city/town level. The response variable was 2015 fatal opioid overdose rate. Explanatory variables (all included in the model initially as both linear and quadratic terms) were taken from American Community Survey 5 year (2010-2014) estimates of sociodemographic characteristics, MDPH Bureau of Substance Abuse Services facility utilization data (2013), MDPH HIV count surveillance data (2011-2013), MDPH Department of Children and Families child abuse service utilization (2011), MDPH mortality data (2012); MDPH STI surveillance counts (2012), and Massachusetts Lab and Workforce Development unemployment rates (March 2016). Statistical significance was determined *a priori* at $p<0.05$. All analyses were performed with R 3.2.3.

GIS
From January to July 2015, a survey was conducted of all 1,042 retail pharmacies in MA regarding over-the-counter naloxone and syringe sales. Addresses for all survey-participating pharmacies and OEND sites were assigned X and Y coordinates using Texas A&M University's online geocoding service (http://geoservices.tamu.edu). Initial descriptive maps were made of 2015 overdose rates by city/town. TIGER shapefiles were used in ArcGIS to create travel-distance maps (set at 5km) for any point known to distribute or sell naloxone (OEND sites and pharmacies). Kernel density estimates were run on overdose counts scattered randomly across city/town polygons to create a fatal opioid-related overdose heat map stratified by decile of overdose density (only areas where overdose density was greater than average (>50th percentile) were depicted on the raster. Areas of higher than average overdose burden that did not overlap with the naloxone travel-distance polygon were determined to be areas of high overdose burden with low naloxone availability, and pharmacies that did not stock naloxone residing inside those areas were identified.

Model residuals were plotted in GIS by standard deviation, indicating towns with higher and lower fatal overdose rates than was predicted by the model. The standard deviation of model residuals was co-plotted with high and low overdose rate towns. Towns with high and low model residuals were identified.

Results

Overdose Rates by City/Town
Overdose rate varied greatly by city/town in MA (Figure 1), and the variation in rate is compounded by the small population size of many towns (106 of 351 city/towns in MA have a population <5,000).

Linear Regression
Of 32 initial model explanatory variables (16 unique variables and quadratic terms for each), 6 significant predictors of city/town fatal opioid-related overdose rate were identified (Table 1). Model fit was marginal (r-squared=0.44). City/towns with model residuals more extreme than -1.5 standard deviations from the residual mean were identified as positive deviants because they had a lower overdose rate than predicted (negative residual) (Table 2). City/towns with model residuals more extreme than 1.5 standard deviations from the residual mean were identified as negative deviants because they had a higher overdose rate than predicted (positive residual) (Table 2). Model residual by city/town was mapped by standard deviation from residual the mean (Figure 2).

Naloxone Availability
809 pharmacies responded to the survey (77% response rate). 365 of 851 pharmacies (43%) reported that they stocked naloxone, and of those 229 (63%) were able to report the amount of naloxone typically stocked, indicating reliable naloxone availability. The statewide coverage of naloxone as measured by 5 kilometer travel distance to a naloxone-stocking pharmacy or OEND site was mapped (Figure 3). Of the 444 non-naloxone-stocking pharmacies, 99 (22%) were outside of 5 kilometer travel distance of another pharmacy that stocks naloxone or OEND site. Of those 99, 55 (12% of all non-naloxone-stocking pharmacies) were located in areas of high overdose burden (overdose Kernel density concentration greater than average) and were further than 5 kilometer travel distance to an OEND site or naloxone-stocking-pharmacy (Figure 4).

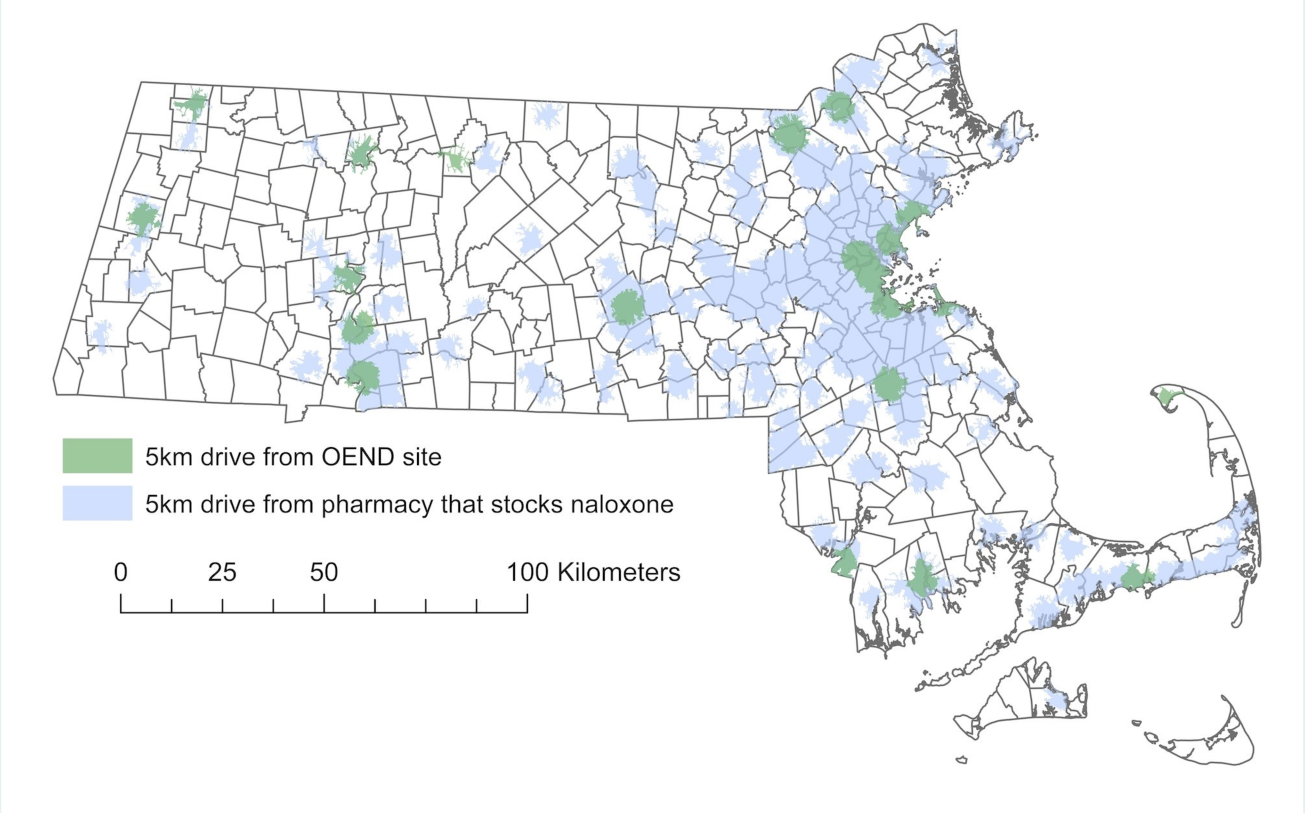

Figure 3. 5 kilometer travel distance from OEND sites and pharmacies that stock naloxone.

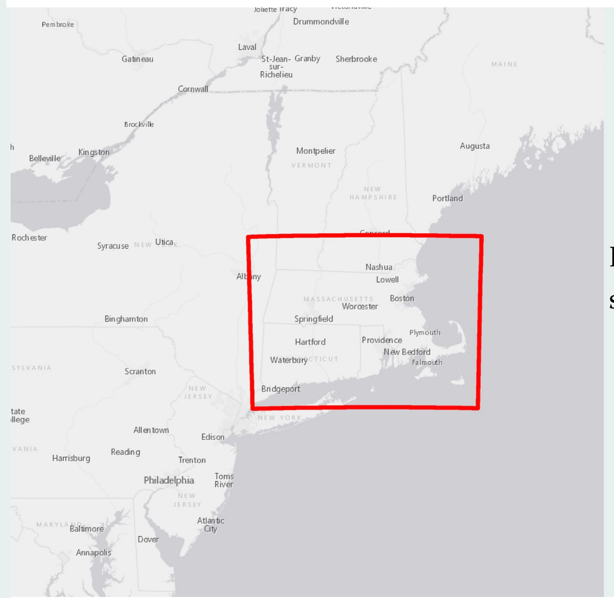

Figure 5. Locator map of Massachusetts.

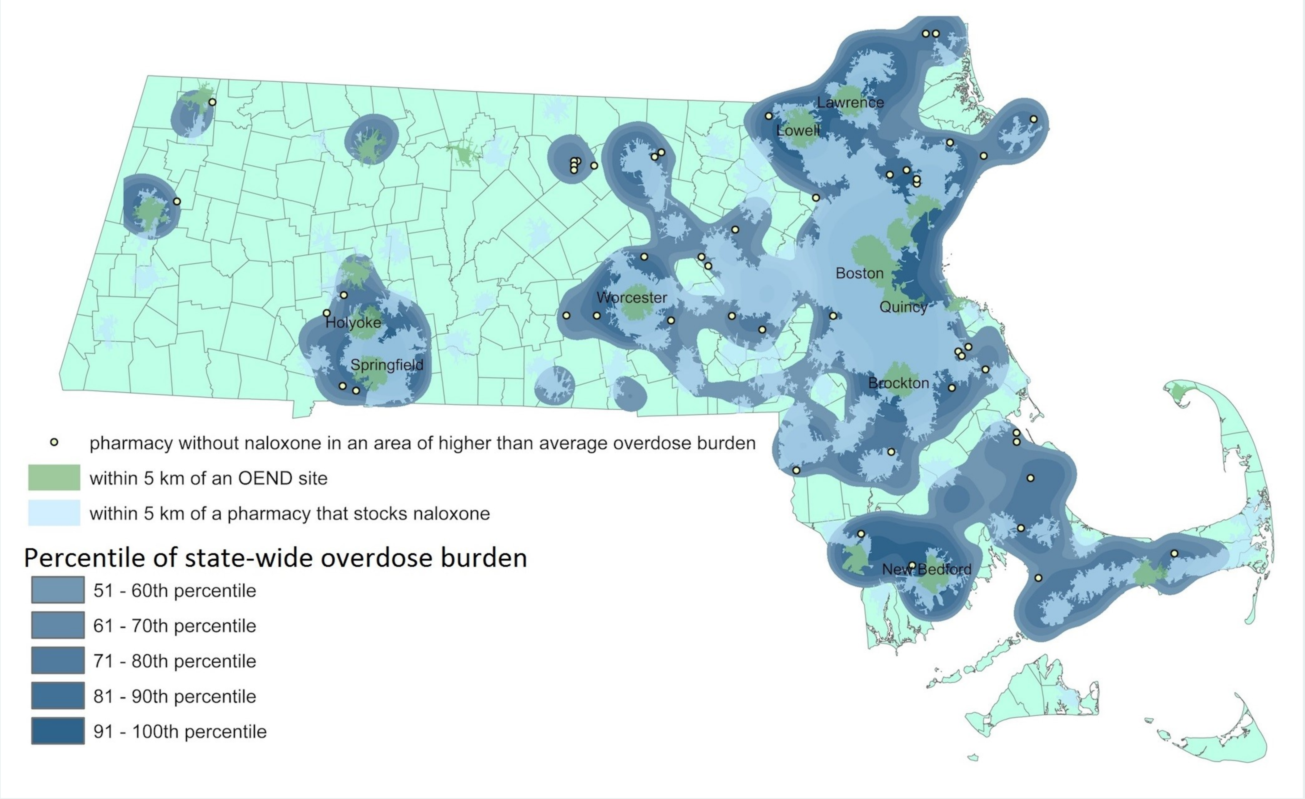

Figure 4. State-wide overdose burden as determined by kernel density of city/town fatal overdose counts scattered randomly in respective city/town polygons. Density reported as percentile of state-wide overdose burden. Pharmacies in areas of higher than average overdose and not inside a 5km drive distance of a naloxone-stocking pharmacy or OEND site are shown.

Model Term	coefficient	p-value
2011-2013 3year average HCV incidence (rate per 100k)	.079	p = 0.03
2013 BSAS intake report of IDU in the past year (rate per 100k)	.028	p < 0.0001
2012 Chlamydia incidence (rate per 100k)	.042	p < 0.01
(2011-2013 3year average HCV incidence (rate per 100k) ^ 2	.00030	p = 0.04
(BSAS Heroin Admission rate per 100k) ^ 2	.00000073	p < 0.0001
(2012 Chlamydia incidence (rate per 100k)) ^ 2	.000034	p = 0.01

Table 1. Final linear regression terms with beta-coefficients and p-values.

Positive Deviant Communities	Residual Standard Deviations	Negative Deviant Communities	Residual Standard Deviations
Great Barrington	-2.26	Spencer	3.22
Dalton	-2.18	Hanson	3.14
Norton	-1.88	Tyngsborough	2.70
Brewster	-1.87	Middleton	2.63
Berkley	-1.85	Mashpee	2.48
Foxborough	-1.63	Rockport	2.40
Winchendon	-1.63	Boxford	2.38
Holyoke	-1.61	Lee	1.86
Dudley	-1.61	Deerfield	1.85
East Bridgewater	-1.60	Harwich	1.75
Saugus	-1.58	Norwell	1.69
		Newbury	1.65
		Maynard	1.59
		Rockland	1.58
		Mattapoisett	1.57
		Canton	1.55
		Middleborough	1.53
		Greenfield	1.51

Table 2. Positive deviant (negative residuals) and positive deviant communities (positive residual) as identified by greater than 1.5 standard deviation model residual. See Figure 2 for a map of these communities.

Discussion

This analysis served two broad purposes. First, pharmacies that were not participating in the statewide naloxone standing order but which were in an area of high overdose burden were identified. The naloxone-stocking decision of these 55 pharmacies (12% of pharmacies which do not stock naloxone) is more powerful than similar pharmacies located in low overdose burden areas. This sets up the possibility of a future focused intervention to re-contact this pharmacy subset to alert them to our findings and measure if this knowledge influences them to change their policy.

Second, in the setting of the state-wide fatal opioid overdose public health emergency and related legislative action, there is increased interest in identifying emerging and persistent geographic clusters of fatal overdose. Though efforts elsewhere focus on predictive analyses utilizing close to real-time data, the model derived here follows in that vein and allowed us to identify positive and negative deviant towns. This deviance may be approached in several ways. First, there is certainly room for more robust model building through the inclusion of other data sources, particularly fentanyl seizures. It is also appropriate to consider this model to be a hypothesis-building exercise, prompting public health practitioners to investigate the positive and negative deviant towns in a more in-depth and qualitative manner to determine what local factors lead them to deviate from the behaviors of other Massachusetts communities.

References

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