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The role of increasing pharmacy and community distributed naloxone in the opioid overdose epidemic in Massachusetts, Rhode Island, and New York City☆

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Abstract

☆All authors report no conflict of interest.

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Contributors

All authors contributed to the design of the study. JRM and CEF wrote the first draft of the manuscript. JRM managed the statistical analysis with assistance from CEF, AJ, and SMM. All authors made contributions to the interpretation of the data including clinical and epidemiological inferences. All authors contributed to the discussion section, revised, and approved the final manuscript.

Declaration of Competing Interests

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

Supplementary materials

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Background: Naloxone distributed to people at risk for opioid overdose has been associated with reduced overdose death rates; however, associations of retail pharmacy-distributed naloxone with overdose mortality have not been evaluated.

Methods: Our analytic cohort uses retail pharmacy claims data; three health departments' community distribution data; federal opioid overdose data; and American Community Survey data. Data were analyzed by 3-digit ZIP Code and calendar quarter-year (2016Q1–2018Q4), and weighted by population. We regressed opioid-related overdose mortality on retail-pharmacy and community naloxone distribution, and community-level demographics using a linear model, hypothesizing that areas with high overdose rates would have higher current levels of naloxone distribution but that increasing naloxone distribution from one quarter to the next would be associated with lower overdose.

Results: From Q1–2016 to Q4–2018, the unadjusted naloxone distribution rate increased from 97 to 257 kits per 100,000 persons, while the unadjusted opioid overdose mortality rate fell from 8.1 to 7.2 per 100,000 persons. The concurrent level of naloxone distribution (both pharmacy and community) was positively and significantly associated with fatal opioid overdose rates. We did not detect associations between change in naloxone distribution rates and overdose mortality.

Conclusion: Naloxone distribution volumes were correlated with fatal opioid overdose, suggesting medication was getting to communities where it was needed most. Amid high rates of overdose driven by fentanyl in the drug supply, our findings suggest additional prevention, treatment, and harm reduction interventions are required—and dramatically higher naloxone volumes needed—to reverse the opioid overdose crisis in the US.

Keywords

Naloxone; Distribution; Opioid overdose

1. Introduction

Opioid overdose rates are increasing at alarming rates in the United States, especially given the increased presence of fentanyl in the illicit drug supply (Colon-Berezin et al., 2019; Gladden et al., 2016; Jalal et al., 2018). Naloxone distribution plays an important role in opioid overdose prevention (Bagley et al., 2017). While prior research has demonstrated the effectiveness of community-based opioid education and naloxone distribution (OEND) programs to reduce opioid overdose in some settings (Walley et al., 2013), less is known about the population effectiveness of pharmacy-distributed naloxone, especially in areas where longstanding OEND programs exist (Oliva et al., 2016). Systematic reviews of naloxone distribution that include non-US jurisdictions are similar, in which effectiveness of general distribution is greatest for populations most at risk (Cherrier et al., 2022), while studies of pharmacy distribution specifically are less common and lack large implementation studies that could demonstrate effectiveness (Nielsen and Van Hout, 2016). Pharmacy distribution of naloxone is supported by standing orders (e.g., dispensed to anyone who requests it, without need of a prescription) and other local policies, and appears to be a successful mechanism to increase the naloxone supply in the community (Abouk et al., 2019; Murphy et al., 2019). One study found the adoption of pharmacy naloxone access

laws (NALs) was associated with about 10% decreased opioid-overdose mortality, while another indicated 14% lower incidence of opioid-overdose mortality (McLellan et al., 2000; Rees et al., 2019). However, we are not aware of any research that examines the marginal effect of both pharmacy and community distributed naloxone on opioid overdose mortality.

Additionally, a bidirectional relationship between naloxone distribution and overdose rates at the community level creates a complex methodological challenge that must be addressed when isolating the impact of naloxone distribution on opioid-related overdose mortality. Specifically, while higher availability of naloxone would be expected to reduce opioid overdose deaths, a worsening opioid overdose epidemic and rising mortality rates (whether due to increased prevalence of use or a more dangerous supply), may prompt public agencies and OEND programs to ramp up distribution, or may encourage more individuals to seek naloxone. This issue is known in the health economics literature as *simultaneity bias*, a form of endogeneity in which an explanatory variable of a regression model is determined simultaneously with the dependent variable of interest. To our knowledge, there have been no identified studies that grappled with this challenge or tested for such a relationship (Naumann et al., 2019).

The northeastern region of the United States, including the jurisdictions of Massachusetts, Rhode Island, and New York City, has struggled with high rates of opioid-related overdose mortality for more than a decade. These three jurisdictions, two of which share a border, have been deeply affected by the rapid increase in fentanyl-related opioid overdoses, and thus have invested heavily in both community- and pharmacy-based naloxone distribution. Two New York City boroughs (Bronx and Staten Island), Massachusetts, and Rhode Island have age-adjusted opioid overdose death rates that are significantly higher than the national average (28.1, 31.8, 33.0, and 30.8 per 100,000 respectively versus a national average of 19.8 per 100,000) (NYC Health, 2017). In response to this epidemic, New York City launched “Healing NYC” in 2017 with a goal to distribute 100,000 naloxone kits per year (Paone et al., 2017). Massachusetts and Rhode Island intend to increase naloxone availability by: continuing to support OEND programs; training first responders; encouraging pharmacy-based naloxone access; dispensing naloxone at community health centers, emergency departments, opioid treatment programs, and correctional centers; and distributing naloxone through street outreach and syringe service programs (Massachusetts Department of Public Health, 2021; Raimondo, 2016). Research that compares the effect of naloxone distribution levels across distinct contexts and programs that differ in their approach is urgently needed to inform future policy.

The objective of this study was to estimate the role that retail pharmacy and community naloxone distribution has on preventing opioid-related overdose deaths in Massachusetts, Rhode Island, and New York City. This study leverages a nationally-representative, detailed, and comprehensive prescription claims data set containing naloxone prescriptions dispensed in a majority of pharmacies, and is the first study we are aware of to use prescription claims data of pharmacy naloxone distribution to estimate its impact on opioid overdose fatalities at the community level. We match these data with comprehensive local community-based naloxone, administrative, and overdose surveillance data, capturing opioid overdose fatalities and OEND activities. We hypothesized that concurrent naloxone distribution will

be positively correlated with opioid overdose rates, while changes in naloxone distribution volume over time will predict fewer opioid-related overdoses in subsequent quarters.

2. Methods

Assessing the role of pharmacy and community naloxone distribution in preventing fatal opioid-related overdoses required merging several datasets from local, federal, commercial, and public sources. We then characterized the change in pharmacy and community naloxone distribution over time alongside the change in fatal opioid overdose rates in Massachusetts, Rhode Island, and New York City. Finally, we measured the association between naloxone distribution—including the absolute number of kits distributed and the quarter-to-quarter change in kit distribution rate—and fatal overdose with a multivariable regression approach. This study was approved and considered exempt by governing Institutional Review Boards as this work involved analysis of aggregate and/or publicly available data.

2.1. Exposure

Our primary exposure was pharmacy and community naloxone distribution, which we obtained from two distinct data sources. First, we used outpatient pharmacy claims from Symphony Health to capture pharmacy-distributed naloxone in the three jurisdictions. The Symphony database captures over 80% of all pharmacies, and 90% of all prescriptions, nationally, has been shown to have good coverage in Massachusetts, Rhode Island, and New York City (work by our team currently under review), and provides dispensing counts by calendar-quarter and 3-digit ZIP Code of the patient (Murphy et al., 2019). Next, we measured community naloxone volume as operationalized by naloxone distributed through Overdose Education and Naloxone Distribution (OEND) programs based on location of the program. These data were provided by the Massachusetts, Rhode Island, and New York City health departments. We measured the per-capita rate of naloxone kits provided through pharmacy and community sources, and aggregated all data to the 3-digit ZIP Code in each calendar quarter by either rolling up from 5-digit ZIP Code in Massachusetts and Rhode Island or mapping borough to 3-digit ZIP in New York City. The 3-digit ZIP was the most granular unit of analysis available following merging the distinct data sources, and we believe using this level of analysis (versus based on state or region of the country) was important to account for local heterogeneity in naloxone distribution and overdose. We had data for 2016–2018 for Massachusetts and Rhode Island and 2017–2018 for New York City. There were 18 3-digit ZIP Code areas in Massachusetts, 2 in Rhode Island, and 10 in New York City (we excluded codes 108 and 110 as they are only partially in the city), yielding 120 ZIP-quarter observations in a given year for which we had data from all three sites.

We parameterized naloxone distribution in the pharmacy and community settings in two ways: 1) quarterly naloxone distribution rate, and 2) the change in naloxone distribution between the prior and current quarter. We hypothesized that the first effect—same quarter naloxone distribution—would reflect the severity of the overdose epidemic (places with more naloxone distribution likely had higher rates of opioid overdose mortality), and that the *change* variable would capture the strength of the response, where we expected a larger

response in terms of increased distribution of naloxone from one quarter to the next to have a larger effect on curbing opioid-related overdose.

2.2. Outcome

Our primary outcome was the rate of fatal opioid-related overdose in each 3-digit ZIP Code, by calendar quarter. We derived these counts from the Multiple Cause of Death national mortality data from the National Center for Health Statistics (NCHS) within the Centers for Disease Control and Prevention (CDC). These data report the underlying cause of death from death certificate data of US residents, based on the 10th revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10 codes). We used an algorithm developed by the Substance Abuse and Mental Health Services Administration to derive opioid-related overdoses using both underlying and multiple cause fields (Substance Abuse and Mental Health Services Administration, 2018). As these data are reported at the county level, we used ZIP-county cross-walks from the United States Department of Housing and Urban Development (HUD) to calculate the number of opioid-related overdoses by 3-digit ZIP Code.

2.3. Weighting strategy

Our exposure and outcome variables were reported as counts in the source data, leading to large differences across ZIP areas given that our data cover both high and low population density areas, such as New York City and Western Massachusetts, respectively. To address this, we weighted both exposure and outcome variables using annual resident population estimates from the Census Bureau (Census.gov, 2020). Like the mortality data, these data were converted from county to 3-digit ZIP level using the HUD crosswalk.

2.4. Demographic characteristics

We used publicly-available data from the American Community Survey (ACS) to include detailed information on age, gender, race, ethnicity, income, and health insurance status by 3-digit ZIP Code for Massachusetts, Rhode Island, and New York City. The values were time-varying by year and 3-digit ZIP Code, and are specific to a community not tied to individuals who received naloxone or those who experienced overdose. Specific ACS datasets used were the “Selected Economic Characteristics, ACS Demographic and Housing Estimates, and Selected Social Characteristics of the United States.” We measured the ACS variables per 10 percentage point change in value.

2.5. Statistical approach

We estimated the association between naloxone distribution and opioid-related overdose using a linear model with 3-digit ZIP Code fixed effects and a linear time trend. The linear model approach best fit our modeling strategy of including a level (current quarter naloxone distribution) and change (first difference of naloxone distribution from one quarter to the next) and allowed us to correctly distinguish these two measures and interpret their effect on overdose. We tested the association using naloxone distribution and distribution stratified by pharmacy or community source. In our regression model, opioid-related overdose per 100,000 persons in a given quarter was a function of: the level of pharmacy and

community naloxone distribution in a given quarter; the change in pharmacy and community naloxone distribution between the current quarter and prior quarter; the opioid-overdose rate in the prior quarter; a time trend (1–12 depending on the quarter and year); a fixed effect for each 3-digit ZIP code, and; ACS community characteristics (the effect of a 10 percentage point increase of the proportion of a given 3-digit ZIP Code that is female, between 25 and 65, non-white, Hispanic, enrolled in public insurance or uninsured, and with a household income under $25,000/year). We tested the robustness of our results by conducting three supplemental analyses: 1) a set of sensitivity analyses using a lag-based approach (incorporating lagged levels of quarterly naloxone distribution); 2) estimating variance inflation factors (VIF) to test for multicollinearity, and 3) performing a regression measuring the associating between non-stratified aggregate naloxone distribution and opioid overdose.

2.6. Endogeneity

Endogeneity occurs when an exposure variables is correlated with the error term in a model: this can happen when both exposure and outcome can affect the other over time (simultaneity or reverse causality) or a variable that is associated with both outcome and exposure is omitted (for example, because it cannot be measured). We expect that our coefficient estimates of naloxone distribution may be subject to both of these endogeneity concerns: simultaneity and omitted variable bias. While we expect that higher availability of naloxone should reduce opioid overdose deaths, a worsening opioid overdose epidemic may prompt a concurrent increase in naloxone demand and supply via both pharmacies and community programs. These effects imply that naloxone distribution and overdose mortality are potentially co-determined, introducing simultaneity bias in the coefficient estimate of interest. In addition, naloxone dispensing rates do not fully account for the existing supply of naloxone in the community, which is a function of past naloxone rates, the utilization of existing naloxone, program catchment area, and rate of disposal over time. The existing supply of naloxone is likely correlated with both overdose mortality and current naloxone distribution rates, thereby introducing omitted variable bias in the regression model. Consequently, it is difficult to distinguish the lifesaving effects of naloxone for individual overdoses from overall increases in naloxone and overdoses that may be occurring in the community. We have attempted to isolate the effect of the response to increasing overdose by modeling the quarter-over-quarter change in naloxone kits distributed, as well as the level of kits distributed. However, absent the use of a good instrument, we may not be completely addressing endogeneity concerns (see Limitations). We attempted to be parsimonious in our variable selection process to exclude “bad controls” that could be in principle affected by the exposure as well (Cinelli et al., 2020). In our example we do not believe that, for example, naloxone distribution would affect community-level demographics. We assess the potential severity of endogeneity by running a reverse regression predicting aggregate naloxone distribution as a function of overdose mortality and relevant control variables. While this is not a “solution” to endogeneity, it allows us to test the hypothesized bidirectional relationship between naloxone distribution and overdose rates.

3. Results

The final analytic dataset included over 10,000 opioid-related deaths and 275,000 naloxone kits distributed between 2016 and 2018. Fig. 1 shows the quarterly rate of opioid-related mortality and pharmacy and community naloxone distribution. Overall, the quarterly unadjusted opioid-related mortality rate fell from an average of 8.1 per 100,000 persons in Quarter 1 of 2016 to 6.8 per 100,000 persons in Quarter 4 of 2018. Over that same period, the unadjusted community and pharmacy naloxone distribution rates more than doubled from 74 community-distributed kits and 23 pharmacy-distributed kits per 100,000 persons to 172 community-distributed and 71 pharmacy-distributed kits per 100,000 persons. We graphed the change in naloxone distribution per 100,000 persons as well, although this did not display a consistent pattern over time (Supplemental Figure 1). In the secondary analysis stratifying by site, we observed a higher opioid overdose mortality rate in Massachusetts and Rhode Island relative to New York City, and found that the rate of naloxone distribution increased the fastest in New York City and Rhode Island relative to Massachusetts (Fig. 2).

Next, we assessed the association between naloxone distribution and opioid-related mortality controlling for geographic-level indicators of sex, age, race, ethnicity, poverty, and insurance status. We found a contemporaneous positive association between same quarter pharmacy and community distributed naloxone and opioid overdose (pharmacy distribution coefficient 0.007 95% confidence interval [CI] 0.001–0.013 and community distribution coefficient 0.005 95% CI 0.002–0.008). Our measure of the change in naloxone distribution, a relatively exogenous measure of the impact of naloxone on mortality, had the hypothesized negative sign, but was not statistically significant at the 5% alpha level (Table 1). The linear time trend was significantly associated with lower mortality, indicating that opioid-related overdose decreased slightly over our study period. We also found that the proportion of a community that was female or Hispanic was associated with higher overdose mortality. Each 10-percentage point increase in the proportion of the population that was female or Hispanic was associated with 19–20 more overdoses per 100,000 person years in each model (Table 1).

Our sensitivity analyses support the robustness of our results. First, our reverse regression found that overdose was significantly associated with naloxone distribution (Supplemental Table 1). This further supports the positive correlation between naloxone distribution and fatal overdose. Second, including lagged indicators of naloxone distribution did not change the interpretation of the results, with the level of naloxone in the current quarter positively associated with overdose death rates: 1 and 2 quarter lagged values were not statistically significant (Supplemental Table 2).

In the model testing the effect of combined naloxone distribution, we found a statistically significant relationship between same quarter distribution and mortality, confirming the contemporaneous positive correlation with mortality and same quarter naloxone (Supplemental Table 3). While not statistically significant, we found the change in naloxone to have a negative sign as hypothesized and as we found for change in community naloxone distribution. Finally, the VIF analysis did not show evidence of severe multicollinearity in our naloxone distribution measures.

4. Discussion

Our novel, multi-jurisdiction assessment of naloxone distribution and overdose mortality includes over 10,000 overdoses and 275,000 naloxone kits distributed, and is among the first attempts to assess the distinct relationships between both pharmacy and community distributed naloxone on opioid overdose mortality in the United States. Between 2016–2018, we observed little change in opioid-related overdose deaths in the three jurisdictions, compared to a rapid increase in naloxone distribution over the same time period. When modeled in a regression analysis, these trends translated to a significant, positive association between same-quarter naloxone distribution and opioid overdose mortality, and no detectable effect of the change in naloxone distribution from one quarter to the next.

These results have several potential explanations. First, our parameterization of naloxone as two functional forms (concurrent volume and quarter-over-quarter change) was meant to represent both the severity of the overdose epidemic generally (we expect places with high overdose rates to have relatively high naloxone distribution), as well as the effect of specific naloxone infusions (the change from one quarter to the next). Based on this, we first hypothesized a positive association between current-quarter naloxone and fatal overdose rates, which was borne out in the regression analysis and bolstered by our finding in the analysis separating pharmacy and community naloxone. We further hypothesized a negative association between the change in naloxone distribution and overdose, which did not materialize in the regression analysis. The descriptive graphs of naloxone distribution and mortality – in which distribution increases rapidly with very small corresponding changes in mortality – speak to this finding. However, including changes in the distribution of naloxone decreases the sample size, and subsequently lowered the statistical power of the analysis. A study at the national level may provide further insight on the impact of the change in pharmacy- and community-based naloxone distribution on mortality rates. Second, we may not expect a large effect *at the population level* of naloxone distribution on opioid overdose mortality; for example, it is possible we would have seen a stronger effect in a more targeted population. This expectation is consistent with prior work demonstrating the cost-effectiveness of naloxone distribution specifically among those at high risk (Acharya et al., 2020), rather than the population at large. While naloxone is pharmacologically effective for reversing opioid overdoses and saving lives, previous research suggests that interventions addressing the underlying cause of the overdose, such as medications for opioid use disorder, are necessary and effective in the long term (Linas et al., 2021). Unless interventions are in place to support those who were rescued from a fatal overdose in managing their use disorder, the risk of a subsequent overdose remains (Morgan et al., 2020a, 2020b).

Findings from our ACS measures indicate that communities with a higher proportion of women and Hispanic individuals are associated with higher levels of fatal overdose. Prior research has demonstrated that non-white individuals with OUD are less likely to access treatment or other harm reduction services due to structural barriers and systemic racism (Hansen et al., 2016). This may result in decreased access to and uptake of naloxone among communities who have historically faced punitive responses to drug-related health issues, rather than compassionate treatment and care (Chatterjee et al., 2022; Rowe et al., 2016).

Future research should investigate how structural racism or practices that create barriers to care for people of color or women may be a source for disparity in the distribution or uptake of naloxone. For example, while a recent study did not find racial/ethnic inequities in naloxone distribution in Massachusetts or Rhode Island on a community level, the study was not able to assess whether the racial/ethnic makeup of people obtaining naloxone was the same as those experiencing overdoses (Nolen et al., 2021). However, while we believe this warrants future study of more effective ways to target naloxone distribution, these ACS measure are community-level indicators, and do not prove association or causation between ethnic or gender identity and overdose on the individual level. Rather, the community-level demographic indicator may be acting as a proxy for other unobserved neighborhood characteristics including socioeconomic factors. It is likely that this relationship is complex and dynamic, and a rich area for future study.

There are several limitations to this work. First, the form of the pharmacy data required aggregation to the 3-digit ZIP area. Smaller geographic areas may have provided us more information with which to detect an effect of naloxone, and understanding the community-level distribution of naloxone and overdose mortality is critical to inform targeted, community-based naloxone distribution strategies (Zang et al., 2021). This effect may be exacerbated by our use of quarter-year, which is broad time measure. It may be useful to replicate this analysis with more granular geographic and time stratification should those data become available. Second, we were limited in the variables we could include in our analysis. Other factors, such as dual prescribing of naloxone alongside opioids, fentanyl penetration, or others, may affect the relationship between naloxone distribution and mortality. We attempted to address this by including both ZIP-level fixed effects to capture between-ZIP differences, and various community-level ACS measures of the composition of each ZIP area. Third, we were unable to capture naloxone distribution happening in emergency departments or through programs not funded by the state/city. Additionally, while the 3-digit ZIP associated with pharmacy distribution reflected a patient's residence, community distribution location was based on the location of the distributing facility. For some community distribution we may be misclassifying the location of distribution if an individual had to travel outside of their 3-digit ZIP to obtain community naloxone. This is mitigated somewhat by the fact that 3-digit ZIP areas are large (for example, Rhode Island only had two), but more granular analysis may be helpful. Fourth, we were not able to control for endogeneity using a more robust instrumental variables approach due to the lack of a good instrument and our short timeframe. For example, while we might expect certain naloxone access laws (Abouk et al., 2019) to act as a good instrument (given the effect of these laws on mortality acts via increases in naloxone distribution), all three jurisdictions had enacted comprehensive naloxone access laws prior to our study timeframe.

5. Conclusion

Over the study period, naloxone distribution increased and was correlated with fatal overdose in three Northeast jurisdictions, indicating that the communities hardest hit by the opioid overdose epidemic also received relatively more naloxone, as is appropriate. However, while naloxone distribution increased and opioid-related mortality decreased over our observation period, we did not detect a statistically significant association between the

change in naloxone distribution and mortality at the population level from quarter to quarter. It is likely that naloxone distribution alone is necessary but not sufficient to reverse the opioid-overdose epidemic in the United States.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

Abouk R, Pacula RL, Powell D, 2019. Association between state laws facilitating pharmacy distribution of naloxone and risk of fatal overdose. JAMA Intern Med 179 (6), 805–811. [PubMed: 31058922]

Acharya M, Chopra D, Hayes CJ, Teeter B, Martin BC, 2020. Cost-Effectiveness of Intranasal Naloxone Distribution to High-Risk Prescription Opioid Users. Value in health : the journal of the International Society for Pharmacoeconomics Outcomes Res. 23(4), 451–460.

Bagley SM, Forman LS, Ruiz S, Cranston K, Walley AY, 2017. Expanding access to naloxone for family members: the Massachusetts experience. Drug Alcohol Rev..

Census.gov, 2020. Decennial Census Datasets.

Chatterjee A, Yan S, Xuan Z, Waye KM, Lambert AM, Green TC, Stopka TJ, Pollini RA, Morgan JR, Walley AY, 2022. Broadening access to naloxone: community predictors of standing order naloxone distribution in Massachusetts. Drug Alcohol Depend. 230, 109190.

Cherrier N, Kearon J, Tetreault R, Garasia S, Guindon E, 2022. Community Distribution of Naloxone: a Systematic Review of Economic Evaluations. Pharmacoecon. Open 6 (3), 329–342. [PubMed: 34762276]

Cinelli C, Forney A, Pearl J, 2020. A Crash Course in Good and Bad Controls. SSRN Electronic J..

Colon-Berezin C, Nolan ML, Blachman-Forshay J, Paone D, 2019. Overdose Deaths Involving Fentanyl and Fentanyl Analogs - New York City, 2000–2017. MMWR Morb. Mortal. Wkly. Rep 68 (2), 37–40. [PubMed: 30653482]

Gladden RM, Martinez P, Seth P, 2016. Fentanyl Law Enforcement Submissions and Increases in Synthetic Opioid-Involved Overdose Deaths - 27 States, 2013–2014. MMWR Morb. Mortal. Wkly. Rep 65 (33), 837–843. [PubMed: 27560775]

Hansen H, Siegel C, Wanderling J, DiRocco D, 2016. Buprenorphine and methadone treatment for opioid dependence by income, ethnicity and race of neighborhoods in New York City. Drug Alcohol Depend. 164, 14–21. [PubMed: 27179822]

Jalal H, Buchanich JM, Roberts MS, Balmert LC, Zhang K, Burke DS, 2018. Changing dynamics of the drug overdose epidemic in the United States from 1979 through 2016. Science 361 (6408).

Linas BP, Savinkina A, Madushani R, Wang J, Yazdi GE, Chatterjee A, Walley AY, Morgan JR, Epstein RL, Assoumou SA, 2021. Projected estimates of opioid mortality after community-level interventions. JAMA Netw. Open 4 (2) e2037259–e2037259. [PubMed: 33587136]

Massachusetts Department of Public Health, 2021. Governor's Opioid Addiction Working Group. https://www.mass.gov/lists/governors-opioid-addiction-working-group. (Accessed 1 October 2021).

McLellan AT, Lewis DC, O'Brien CP, Kleber HD, 2000. Drug dependence, a chronic medical illness: implications for treatment, insurance, and outcomes evaluation. JAMA 284 (13), 1689–1695. [PubMed: 11015800]

Morgan J, Barocas JA, Murphy SM, Epstein RL, Stein MD, Schackman BR, Walley AY, Linas BP, 2020a. Comparison of rates of overdose and hospitalization after initiation of medication for opioid use disorder in the inpatient vs outpatient Setting. JAMA Netw. Open 3 (12), e2029676. [PubMed: 33320266]

Morgan J, Wang J, Barocas JA, Jaeger JL, Durham NN, Babakhanlou-Chase H, Bharel M, Walley AY, Linas BP, 2020b. Opioid overdose and inpatient care for substance use disorder care in Massachusetts. J. Subst. Abuse Treat 112, 42–48. [PubMed: 32199545]

Murphy SM, Morgan JR, Jeng PJ, Schackman BR, 2019. Will converting naloxone to over-the-counter status increase pharmacy sales? Health Serv. Res 54 (4), 764–772. [PubMed: 30790269]

Naumann RB, Durrance CP, Ranapurwala SI, Austin AE, Proescholdbell S, Childs R, Marshall SW, Kansagra S, Shanahan ME, 2019. Impact of a community-based naloxone distribution program on opioid overdose death rates. Drug Alcohol Depend 204, 107536.

Nielsen S, Van Hout MC, 2016. What is known about community pharmacy supply of naloxone? A scoping review. Int. J. Drug Policy 32, 24–33. [PubMed: 26949189]

Nolen S, Zang X, Chatterjee A, Behrends CN, Green TC, Kumar A, Linas BP, Morgan JR, Murphy SM, Walley AY, Yan S, Schackman BR, Marshall BDL, 2021. Community-based naloxone coverage equity for the prevention of opioid overdose fatalities in racial/ethnic minority communities in massachusetts and rhode island. Addiction.

NYC Health, 2017. Unintentional Drug Poisoning (Overdose) Deaths in New York City, 2000 to 2016 [PDF]. https://www1.nyc.gov/assets/doh/downloads/pdf/epi/databrief89.pdf. (Accessed 12 May 2020).

Oliva EM, Nevedal A, Lewis ET, McCaa MD, Cochran MF, Konicki PE, Davis CS, Wilder C, 2016. Patient perspectives on an opioid overdose education and naloxone distribution program in the U.S. department of veterans affairs. Subst. Abus 37 (1), 118–126. [PubMed: 26675643]

Paone D, Nolan M, Tuazon E, Blachman-Forshay J, 2017. Unintentional Drug Poisoning (Overdose) Deaths in New York City, 2000–2016. New York City Department of Health and Mental Hygiene: Epi Data Brief 89.

Raimondo G, 2016. Rhode Island Overdose Prevention and Intervention Task Force Action Plan [PDF]. http://www.governor.ri.gov/documents/press/051116.pdf. (Accessed 10 May 2020).

Rees DI, Sabia JJ, Argys LM, Dave D, Latshaw J, 2019. With a little help from my friends: the effects of good samaritan and naloxone access laws on opioid-related deaths. J. Law Econ 62 (1), 1–27.

Rowe C, Santos GM, Vittinghoff E, Wheeler E, Davidson P, Coffin PO, 2016. Neighborhood-level and spatial characteristics associated with lay naloxone reversal events and opioid overdose deaths. J. Urban Health 93 (1), 117–130. [PubMed: 26800987]

Substance Abuse and Mental Health Services Administration, 2018. Using International Classification of Diseases (ICD) Codes to Assess Opioid-Related Overdose Deaths https://mnprc.org/wp-content/uploads/2019/01/using-icd-10-codes-to-assess-opioid-related-overdose-deaths.pdf.

Walley AY, Xuan Z, Hackman HH, Quinn E, Doe-Simkins M, Sorensen-Alawad A, Ruiz S, Ozonoff A, 2013. Opioid overdose rates and implementation of overdose education and nasal naloxone distribution in Massachusetts: interrupted time series analysis. BMJ 346, f174. [PubMed: 23372174]

Zang X, Macmadu A, Krieger MS, Behrends CN, Green TC, Morgan JR, Murphy SM, Nolen S, Walley AY, Schackman BR, Marshall BD, 2021. Targeting community-based naloxone distribution using opioid overdose death rates: a descriptive analysis of naloxone rescue kits and opioid overdose deaths in Massachusetts and Rhode Island. Int. J. Drug Policy 98, 103435.

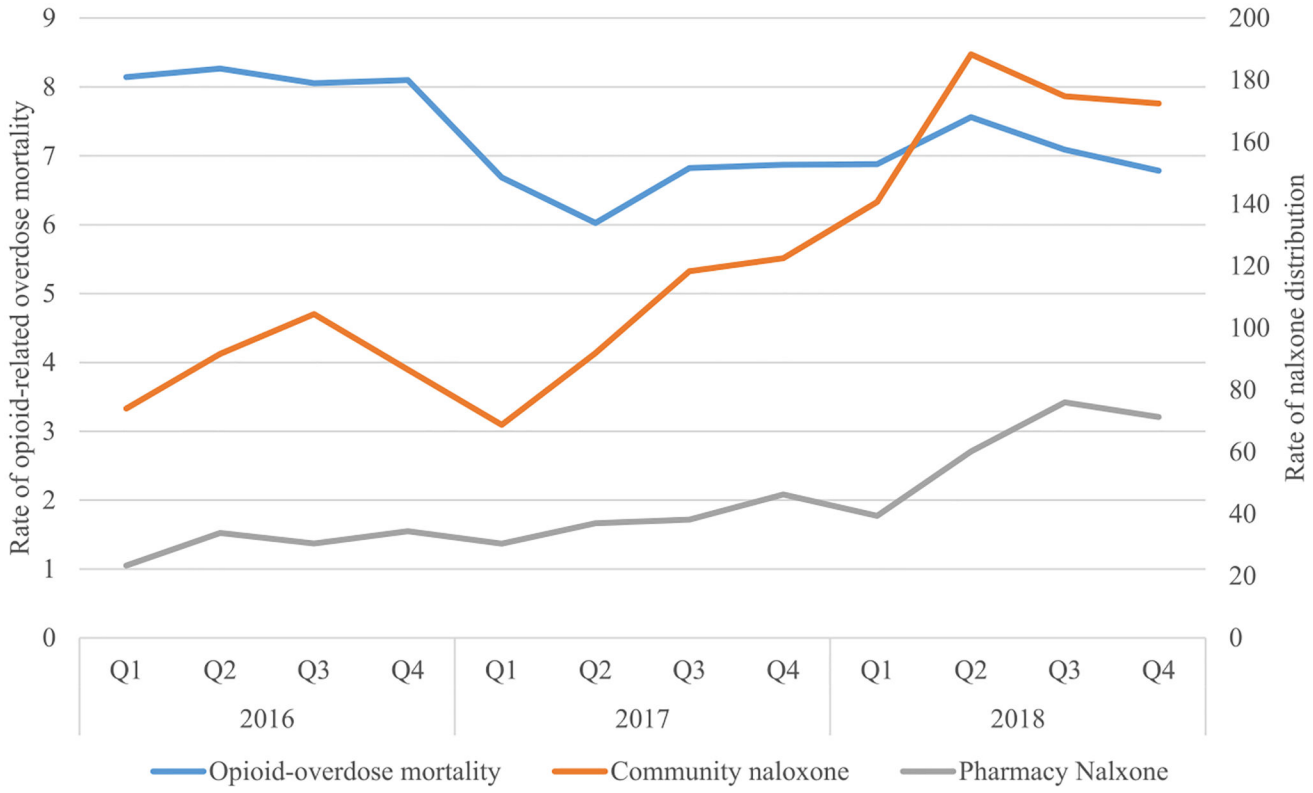

Fig. 1.

Opioid-related overdose mortality and naloxone kit distribution per 100,000 individuals from 2016 to 2018 in Massachusetts, Rhode Island, and New York City.

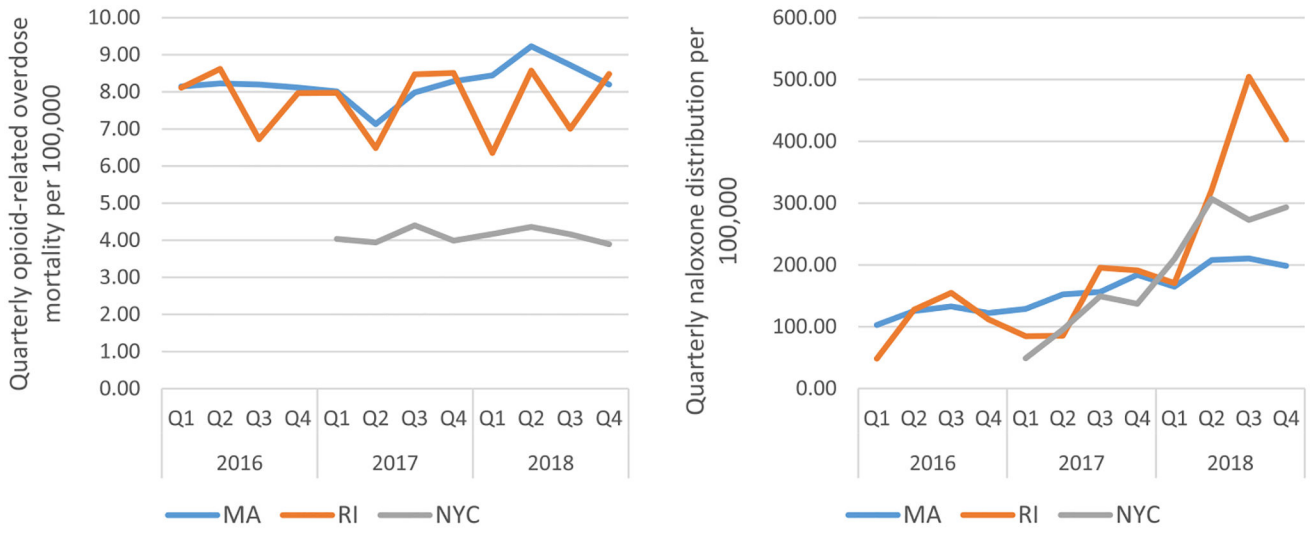

Fig. 2.

Quarterly opioid-related overdose mortality and naloxone kit distribution per 100,000 individuals from 2016 to 2018 stratified by jurisdiction.

Table 1

Regression models predicting the rate of opioid overdose mortality in a community as a function of total and stratified naloxone distribution by programs and pharmacies in the same community.

	Coefficient	Standard error	p-value	95% CI
Prior quarter mortality	−0.0260	0.064	0.686	(−0.1522, 0.1002)
Same quarter pharmacy naloxone distribution	0.0071	0.003	0.026	(0.0008, 0.0133)
Same quarter community naloxone distribution	0.0047	0.002	0.003	(0.0016, 0.0079)
Change in pharmacy distribution from prior quarter	−0.0049	0.004	0.200	(−0.0125, 0.0026)
Change in community distribution from prior quarter	−0.0003	0.002	0.862	(−0.0037, 0.0031)
Linear time trend	−0.1405	0.067	0.038	(−0.2730, −0.0081)
ACS time-varying ZIP-level characteristics (per 10 percentage point change)				
Proportion female	19.3303	8.684	0.027	(2.2266, 36.4339)
Proportion adult 25–64	3.3869	7.279	0.642	(−10.9505, 17.7243)
Proportion non-white	−2.3817	1.492	0.112	(−5.3199, 0.5564)
Proportion Hispanic	20.0830	6.039	0.001	(8.1888, 31.9772)
Proportion with public insurance	−0.7544	1.565	0.630	(−3.8367, 2.3279)
Proportion uninsured	−5.7159	5.227	0.275	(−16.0109, 4.5790)
Proportion of households < $25,000/year	0.0000	0.000	0.123	(0.0000, 0.0000)