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RESEARCH

Opioid overdose rates and implementation of overdose education and nasal naloxone distribution in Massachusetts: interrupted time series analysis

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Abstract

Objective To evaluate the impact of state supported overdose education and nasal naloxone distribution (OEND) programs on rates of opioid related death from overdose and acute care utilization in Massachusetts.

Design Interrupted time series analysis of opioid related overdose death and acute care utilization rates from 2002 to 2009 comparing community-year strata with high and low rates of OEND implementation to those with no implementation.

Setting 19 Massachusetts communities (geographically distinct cities and towns) with at least five fatal opioid overdoses in each of the years 2004 to 2006.

Participants OEND was implemented among opioid users at risk for overdose, social service agency staff, family, and friends of opioid users.

Intervention OEND programs equipped people at risk for overdose and bystanders with nasal naloxone rescue kits and trained them how to prevent, recognize, and respond to an overdose by engaging emergency medical services, providing rescue breathing, and delivering naloxone.

Main outcome measures Adjusted rate ratios for annual deaths related to opioid overdose and utilization of acute care hospitals.

Results Among these communities, OEND programs trained 2912 potential bystanders who reported 327 rescues. Both community-year strata with 1-100 enrollments per 100 000 population (adjusted rate ratio 0.73, 95% confidence interval 0.57 to 0.91) and community-year strata with greater than 100 enrollments per 100 000 population (0.54, 0.39 to 0.76) had significantly reduced adjusted rate ratios compared with communities with no implementation. Differences in rates of acute care hospital utilization were not significant.

Conclusions Opioid overdose death rates were reduced in communities where OEND was implemented. This study provides observational evidence that by training potential bystanders to prevent, recognize, and respond to opioid overdoses, OEND is an effective intervention.

Introduction

Poisoning, nine out of 10 of which are related to drug overdoses,[1] has surpassed motor vehicle crashes to be the leading cause of death by injury in the United States.[2] Overdose is also a major cause of death in Canada,[3] Europe,[4] Asia,[5][6] and Australia.[7] In the United States, increases in fatal overdose since the mid-1990s have been driven by the growth in prescriptions for opioid analgesics[8] and their non-medical use.[9][10] Opioid related emergency department visits and admissions to hospital have increased over the same period.[11] In Massachusetts, since

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Map of the 19 communities in Massachusetts
  coefficients for covariates in adjusted absolute and relative models of opioid overdose related unintentional deaths
  coefficients for covariates in adjusted absolute and relative models of opioid related acute care utilizations
Control models of OEND implementation and ratio of opioid related overdose deaths to cancer deaths
Control models of OEND implementation and ratio of opioid related acute care utilizations to motor vehicle crash acute care utilizations

2005, annual opioid-related overdose deaths have exceeded motor vehicle deaths.[12]

Strategies have been implemented to deal with opioid overdose. Prescription drug monitoring programs,[13] prescription drug take back days, safe opioid prescribing guidelines, and education programs seek to reduce opioid misuse and/or diversion to people who do not have prescriptions. While these strategies are promising, none has been demonstrated in clinical trials or controlled observational studies to reduce overdose rates. Methadone maintenance treatment[14 15] and supervised injection facilities[16] are strategies associated with decreased fatalities from overdose in controlled studies.

Naloxone is an opioid antagonist that reverses the effects of opioid overdose. Overdose education and naloxone distribution (OEND) programs tackle overdose by educating people at risk for overdose and bystanders in how to prevent, recognize, and respond to an overdose. Participants in the program are trained to recognize signs of overdose, seek help, rescue breathe, use naloxone, and stay with the person who is overdosing. From 1996 through 2010, over 50 000 potential bystanders were trained by OEND programs in the United States, resulting in over 10 000 opioid overdose rescues with naloxone.[17] In March 2012, the United Nations Commission on Narcotic Drugs recognized overdose as a global public health issue that warrants focus by the World Health Organization and member countries, including the use of naloxone for the prevention of opioid overdose.[18] Studies of OEND programs have demonstrated feasibility,[19-22] increased knowledge and skills,[23-26] and a concomitant reduction in fatal overdoses after initiation of OEND.[27 28] A controlled study of OEND and overdose rates has not been completed. Implementation of OEND in Massachusetts in communities with a high burden of opioid overdose created the opportunity to study the impact of OEND on opioid related fatal overdose and acute care hospital utilization rates, using high burden communities with low or no OEND implementation as concurrent controls.

Methods

We conducted an interrupted time series analysis of annual opioid related rates of overdose fatalities and utilization of acute care hospitals comparing communities and years where OEND was implemented with those where it was not. The analysis was conducted at the city/town level. Massachusetts consists of 351 geographically distinct cities and towns (referred to as communities). We included the 19 communities with five or greater opioid related unintentional or undetermined intentional fatal poisonings in each year from 2004 to 2006, which were the years immediately preceding the implementation of OEND.

The Massachusetts OEND program

In 2006-07, two community public health agencies began providing OEND.[20] The Massachusetts Department of Public Health expanded the program to four more organizations in 2007 and two more in 2009. These agencies, which provided HIV education and prevention services to substance users, provided OEND to potential overdose bystanders through trained non-medical public health workers under a standing order from the OEND medical director. Potential overdose bystanders were opioid users at risk for overdose, as well as social service agency staff, family, and friends of opioid users. Training sites included syringe access programs, HIV education drop-in centres, addiction treatment programs, emergency and primary healthcare settings, and community meetings, such as support groups for family members of opioid users.

Training curriculums were initially developed by the Harm Reduction Coalition and the Chicago Recovery Alliance,[19 21 27] and adapted for nasal naloxone. OEND trainers completed a four hour course, knowledge test, and two trainings of potential bystanders supervised by a master trainer. The training of program participants by OEND trainers were conducted in groups or individually, took as little as 10 minutes for enrollees with substantial pre-existing knowledge and as much as 60 minutes for groups that generated discussion or had enrollees without prior knowledge of overdose, and were tailored to the training setting. Key elements included minimizing the risk of overdose by reducing polysubstance misuse (for example, concomitant alcohol, benzodiazepine, or cocaine), accounting for reduced tolerance after abstinence, and not using alone; recognizing overdose by assessing for unresponsiveness and decreased respirations; and responding to an overdose by seeking help, providing rescue breathing, administering nasal naloxone, and staying with the person until medical personnel arrived or the person recovered. Trainings concluded with enrollees demonstrating proper assembly of the naloxone device and how naloxone should be administered. Naloxone rescue kits contained instructions, two prefilled syringes with 2 mg/2 mL naloxone hydrochloride, and two mucosal atomization devices. Two doses were included in case one dose was not sufficient or if overdose symptoms returned, because the half-life of many opioids is longer than that of naloxone.

Data collection and measures
Fatal opioid overdose rates

For the fatal opioid overdose outcome, we calculated rates of unintentional and undetermined intentional opioid related drug poisonings by community of residence using in-state occurrent deaths from the electronic database maintained by the Massachusetts Registry of Vital Records and Statistics, Massachusetts Department of Public Health. Death certificates on fatal poisonings in Massachusetts are completed through a single centralized, statewide office of the chief medical examiner, where they are required by law to be reported. Opioid related deaths were defined by ICD-10 (international classification of diseases, 10th revision) codes indicating unintentional or undetermined intentional poisoning (X40-X44, Y10-Y14) in the underlying cause of death field and an opioid specific T code of T40.0-T40.4 and/or the narcotic T code T40.6 in any of the multiple cause of death fields. The use of T40.6 to identify opioid related deaths is recommended in jurisdictions where a high proportion of deaths with this code is opioid specific.[29] An unpublished review of 2007 Massachusetts death certificate literals indicated that T40.6 had a positive predictive value of 98% for an opioid related death. Furthermore, 96.7% of unintentional or undetermined intentional deaths by poisoning in Massachusetts in 2007 received at least one ICD-10 code in the range (T36-T50.8), indicating that specific information on agent or class of agent was present on death certificates for nearly all drug related deaths.

Opioid overdose related acute care hospital utilization rates

We used the Massachusetts inpatient hospital and outpatient emergency department discharge databases administered by the Massachusetts Division of Health Care Finance and Policy to quantify acute care hospital inpatient and emergency department discharges associated with opioid poisoning by city or town of residence. Submission of external cause of injury codes (E codes) are required by state regulation on all cases with a

principle diagnosis of injury or poisoning, ensuring high quality data for state injury surveillance. Cases were defined as discharges having an ICD-9-CM (international classification of diseases, ninth revision, clinical modification) code of one or more of the following opioid related discharge diagnosis or E codes: 965 (.00, .01, .02, .09), E850 (.0, .1, .2). We excluded those cases receiving an E code indicating that the poisoning was the result of intentional self harm, assault, an adverse effect of a drug in therapeutic use, or legal intervention. To avoid duplicate counts with the fatality measure we excluded deaths occurring during the hospital event from this outcome.

Descriptive variables from enrollment and naloxone rescue attempt questionnaires

The Massachusetts Department of Public Health OEND program database included information from program questionnaires collected at both enrollment and whenever an enrollee requested an additional naloxone kit. The completed questionnaires were scanned by form reading software and entered into the program database. At enrollment, zip code of residence, drug use history, and overdose history were collected. We defined users as participants who reported active use or being in treatment or in recovery. Non-users were all other participants, typically social service agency staff, family, and friends of opioid users. A questionnaire was completed when a participant requested a naloxone refill because naloxone had been used during an overdose rescue. Staff were trained to define an overdose when administering the questionnaire as an episode when an individual was unresponsive and had signs of respiratory depression after using substances. We only counted events where participants reported their own overdose rescue attempts if another person administered the naloxone. Self administered naloxone was rarely reported and was not counted as a rescue attempt because a person able to self administer the drug was not considered to be unresponsive. We considered naloxone to be successfully administered if the person's unresponsiveness and respiratory depression improved. Other descriptive variables included the zip code of the place in which the overdose occurred, relationship to the person who overdosed, setting (public or private), number of naloxone doses used, whether naloxone was successful, emergency medical system involvement, rescue breathing, and staying with the person who overdosed.

Independent variables: OEND enrollment rates

To determine the cumulative enrollment rates for the 19 communities with high overdose burdens we used the community of residence based on the zip code of residence on the enrollment questionnaire. We modeled OEND implementation in two ways. Firstly, we categorized OEND implementation into three groups within each year based on the median cumulative enrollment rate (relative model). Groups included community-year strata with no implementation, those below the median (low implementers), and community-year strata with enrollment rates above the median (high implementers). Secondly, to determine if an absolute population density of enrollment was associated with overdose rates, we categorized communities in each year into three categories based on cumulative enrollment rate levels of no implementation, 1-100 per 100 000 population and >100 per 100 000 population (absolute model). In the models we used enrollment cut points of 0, 1-75, >75 and in sensitivity analyses cut points of 0, 1-150, and >150.

Covariates

To account for geographic differences in overdose risk, we adjusted our analyses for demographics. We linearly interpolated community specific data (age, sex, race or ethnicity, poverty) for each year from the community specific 2000[30] and 2010[31] US Census Bureau data.

We used data from the Massachusetts prescription drug monitoring program to adjust for opioid prescriptions to "doctor shoppers," defined as individuals who had schedule II opioid prescriptions from four or more prescribers and filled prescriptions at four or more pharmacies in a 12 month period.[32] We calculated the proportion of schedule II opioid prescriptions dispensed to doctor shoppers per total opioid prescriptions for each community-year stratum.

Inpatient medically supervised withdrawal (detox) results in a period of abstinence that can increase overdose rates,[33 34] whereas engagement in methadone treatment results in decreased rates of overdose.[14] Office based buprenorphine treatment expanded during the study period. To adjust for these three treatment services, we calculated population rates of methadone maintenance, buprenorphine maintenance, and detox events for each community-year stratum using data from the Massachusetts Department of Public Health Bureau of Substance Abuse Services treatment database. Any treatment program licensed by and contracted with the Substance Abuse Services was required to report admission and discharge information.

We accounted for linear trends over the study period by using a time variable T, expressed as 1 for the index year 2002 and increasing in integer increments for each year of the study period.

Statistical analysis

For the interrupted time series we used the annual rates of fatal opioid related overdose and acute care hospital utilization associated with non-fatal opioid overdose by community of residence for the units of analysis. The denominators were the community population based on US Census estimates. Based on the independent variable definitions, we coded individual community-year combinations with an indicator variable denoting "implementation." As in other studies of injury trends[35] and program implementation,[36] we used Poisson regression models to test our hypotheses that those community-year strata with higher implementation would have lower rates. We modeled rates directly with a log-linear statistical model by including counts as the dependent outcome and population at risk as an offset term. We controlled for community level covariates by including them in the model. All hypothesis tests used a significance level (α) of 0.05. We performed regression diagnostics, including quasi likelihood information criteria,[37] to assess goodness of fit. Based on these, we chose first order autoregressive covariance structure to account for the interdependence of repeated measures.

To determine whether our findings were specific to overdose outcomes or due to an unmeasured health system effect, such as healthcare reform, we conducted additional sensitivity analyses. We refit the adjusted Poisson fatal overdose models substituting fatal opioid overdose rates with overdose death to cancer death rate ratios for each community-year stratum using data from the Massachusetts Registry of Vital Records and Statistics. We also refit models substituting acute care utilization rates associated with non-fatal opioid related poisoning with non-fatal opioid related poisoning or non-fatal motor vehicle traffic related injury rate ratio for each community-year stratum.[38] To define cancer deaths we used ICD-10 codes

C000-C979, representing malignant neoplasms. We defined cases of non-fatal motor vehicle traffic related injury by discharge diagnoses with an ICD-9-CM code of 800-909.2, 909.4, 909.9, 910-994.9, 995.5-995.59, 995.80-995.85 and an E code, E810-E819 (.0-.9), for unintentional motor vehicle traffic crash. All analyses were done using SAS version 9.3.

Results

Table 1⇓ lists the characteristics of the 19 communities in Massachusetts. These make up about 30% of the state population and contribute almost half of Massachusetts' fatal opioid overdoses and acute care hospital utilizations for non-fatal opioid overdose.

Between 18 September 2006 and 31 December 2009 in Massachusetts, 4857 individuals were enrolled in OEND and 545 naloxone rescue attempts reported. Among the 19 communities meeting the study criteria, 2912 individuals were enrolled (table 2⇓) and 327 rescue attempts made (table 3⇓). The experience of witnessing an overdose was common among both users and non-users at enrollment. Users commonly had a personal history of overdose and reported detoxification treatment and incarceration in the past year.

Of 327 rescue attempts using naloxone reported by 212 individuals, 87% (286/327) were reported by users. Most rescue attempts occurred in private settings. The rescuer and the person who overdosed were usually friends. Naloxone was successful in 98% (150/153) of the rescues attempts. For the three rescue attempts where naloxone was not successful, the people who overdosed received care from the emergency medical system and survived.

Among the 19 communities studied, none had any OEND implementation in 2002-05, 7 had some implementation in 2006 (median of 3 enrollees per 100 000 population), 14 had some in 2007 (median of 7 enrollees per 100 000), and all 19 had OEND implementation in 2008-09 (medians of 55 and 142, respectively). Figures 1⇓ and 2⇓ show the unadjusted rates of unintentional opioid related overdose deaths and acute acre utilizations, respectively, categorized by no, low and high implementation.

Adjusted models: OEND implementation and fatal overdose rates

Generally, opioid related death rates were reduced in those communities that implemented OEND compared with community-year strata with no OEND implementation. In the adjusted model based on absolute numbers of enrollments, both the low implementer community-year strata with 1-100 enrollments per 100 000 population (adjusted rate ratio 0.73, 95% confidence interval 0.57 to 0.91) and the high implementer community-year strata with greater than 100 enrollments per 100 000 population (0.54 0.39 to 0.76) had significantly reduced adjusted rate ratios in a dose related fashion compared with communities with no implementation (table 4⇓, for full models see supplementary tables 4a and 4b). In sensitivity analyses, using alternative cut points of 75 enrollments and 150 enrollments per 100 000 population, rate ratios were similar. For the adjusted model that used the median enrollment rates, overdose death rates were reduced, but significantly so only for the low implementer group (0.71, 0.57 to 0.90).

Adjusted models: OEND implementation and opioid related non-fatal acute care hospital utilizations

For non-fatal opioid overdose related acute care hospital utilizations, there was no statistically significant association between the communities based on absolute or relative enrollment rates compared with no implementation (table 5⇓, for full models see supplementary tables 5a and 5b). In sensitivity analyses, rate ratios were similar then alternative cut points of 75 enrollments and 150 enrollments per 100 000 population were used.

Control models

Models in which the opioid related overdose fatality outcome were substituted for the ratio of opioid related overdose death rates over the cancer related death rates had statistically significant associations in a similar pattern to the original models. Thus the associations of OEND implementation with fatal overdose rates occurred independently of any effects related to cancer fatalities (see supplementary table 6). The similar procedure with motor vehicle crash injuries and acute care utilization models showed no association of OEND implementation on rates, independent of motor vehicle injuries (see supplementary table 7).

Discussion

Between 2006 and 2009, Massachusetts overdose education and nasal naloxone distribution (OEND) programs trained thousands of people who use opioids and their families, friends, and social service providers to prevent, recognize, and respond to overdoses, resulting in hundreds of reported rescue attempts. Compared with no implementation, both low and high implementation of OEND were associated with lower rates of opioid related deaths from overdose, when adjusted for demographics, utilization of addiction treatment, and doctor shopping (schedule II opioid prescriptions from ≥4 prescribers and filled prescriptions at ≥4 pharmacies in a 12 month period). These associations were seen independently of effects related to cancer death rates. Rates of opioid related visits to an emergency department and admission to hospital were not significantly different in communities with low or high implementation of OEND.

Strengths and limitations of the study

The major strength of this study was the interrupted time series analysis approach that capitalized on naturally occurring geographic and time controls owing to the broad but variable implementation of OEND in Massachusetts. The study included years 2002-09, yet OEND implementation began in some communities in 2006 and gradually expanded through 2009. Thus the "no implementation" comparison group included all 19 communities for 2002-05 and only those communities with no enrollment in 2006-09. The pre-implementation and post-implementation comparisons (no versus any implementation) hinged on when implementation started in an individual community. Further, we investigated effects among those communities with high and low implementation. When implementation was defined in a relative manner, based on the median implementation rate in each year, there was an association in the expected direction, but there did not seem to be an implementation dose relation with opioid related overdose death rates. Yet when implementation was defined in an absolute manner based on the cumulative number of enrollments per population, there was both an association in the expected

direction and a dose relation with death rates. A community's absolute enrollment rate had a stronger impact on overdose death rates than the relative enrollment rate. We included both a disease specific mortality and healthcare utilization outcome. We repeated the analyses with substitute outcomes that incorporated unrelated conditions to check if there was some system level effect in how deaths or acute care utilizations were coded that could account for our findings.

Using an observational approach, this study cannot prove definitively that OEND caused a reduction in opioid related overdose death rates. This study had several other limitations to the data available, which we attempted to address. Firstly, the true population of opioid users in each community was not known. To account for this we adjusted analyses for differences in demographics, use of addiction treatment, and proportion of prescriptions to doctor shoppers. Secondly, opioid overdose fatalities may have been misclassified. However, in Massachusetts the medical examiner's office is centralized, with each death certificate processed through the same system. Thirdly, visits to emergency departments and admissions to hospitals associated with opioid poisoning were defined based on administrative discharge codes. Although discharge codes are a blunt measure of cause for utilization, systematic directional misclassification has not been found in other studies.[39] Fourthly, overdoses may have occurred in clusters, which could result in the assumption that spurious events represent a trend. However, this study was conducted over eight years in 19 communities. Fifthly, we created measures of OEND implementation consistent with our conception of how OEND may impact on rates of fatal overdose and acute care utilization, but they have not been validated in other populations. We tested several levels of OEND implementation and found similar patterns of association with opioid related overdose and acute care utilization rates. Lastly, the description of reported overdose rescue attempts was limited to only those rescues reported back to programs, and thus was likely underreported.

Interpretation

This study provides observational evidence that OEND is an effective public health intervention to address increasing mortality in the opioid overdose epidemic by training potential bystanders to prevent, recognize, and respond to opioid overdoses. OEND implementation seemed to have a dose related impact, where the higher the cumulative rate of OEND implementation, the greater the reduction in death rates. While OEND programs should reduce visits to emergency departments and hospital admissions by preventing overdoses in the first place, they may also increase visits by encouraging bystanders to engage the emergency medical system, which is an explicit part of OEND curriculums. This balance of reducing and increasing the use of the emergency medical system may be why no association was found for acute care utilization.

Implications for research, policy, and practice

Some research issues follow from this study. Because OEND targets not only the overdose risk behaviours of the trainee but empowers trainees to intervene in another person's overdose, it makes a fuller impact at the community level rather than at the individual level. Therefore, an individual level prospective clinical trial is unlikely to capture the community level effect of OEND unless it uses a multisite or social network design or measures community level outcomes to account for the network effects and potential contamination between individual participants. It is also important to determine how OEND should be tailored and implemented among different populations to maximize effectiveness. In Massachusetts, similar OEND curriculums have been delivered to heroin users, prescription opioid users, patients in emergency departments, people who are incarcerated, family members, social service providers, police officers, and fire fighters.

This study provides strong support for the public health agency policy and community based organisation practice to implement and expand OEND programs as a key way to address the opioid overdose epidemic. Two features of the Massachusetts OEND programs that supported broad implementation include the use of an nasal naloxone delivery device and the use of a standing order issued by the health department, which allowed non-medical personnel to deliver OEND. These features may enable broader implementation with greater impact as more communities implement OEND.

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What is already known on this topic

Opioid overdose is a major, expanding cause of preventable death in many countries

Education about overdose and naloxone distribution is an innovative, community based response deployed in many settings that has not been examined in controlled studies

What this study adds

Death rates from opioid overdose were reduced in communities where overdose education and naloxone distribution was implemented compared with not implemented

This provides observational evidence that an overdose education and nasal naloxone distribution program is an effective public health intervention to address the epidemic of fatal opioid overdose

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Tables

Table 1| Characteristics of 19 Massachusetts communities* with high opioid overdose burden. Values are percentages unless stated otherwise

Characteristics	Communities (n=19)
2005 population, total	2 055 086
Mean	108 162
Median	87 392
Range	30 236-609 690
Age <18 years	22.4
Male	48.0
Race or ethnicity:	
Hispanic	13.8
White, non-Hispanic	63.9
Black, non-Hispanic	11.9
Other, non-Hispanic	10.1
Below poverty level	16.4
Treatment events per 100 000 people, 2009:	
Inpatient detoxification	630.0
Methadone maintenance	161.8
Stated funded buprenorphine maintenance	41.5
Opioid prescriptions to doctor shoppers†	10.9

*Geographically distinct cities and towns.

†Schedule II opioid prescriptions dispensed to doctor shoppers (individuals with schedule II opioid prescriptions from ≥4 prescribers and filled prescriptions at ≥4 pharmacies in 12 month period) per total opioid prescriptions dispensed.

Table 2| Characteristics of potential overdose bystanders trained in overdose education and nasal naloxone distribution program in 19 Massachusetts communities*, 2006-09. Numbers are percentages (number/number in group) unless stated otherwise

Characteristics	All enrollees (n=2912)	Users† (n=2007)	Non-users (n=905)
Mean (SD) age (years)	38.1 (12.1)	36.1 (11.1)	42.6 (13.0)
Female and male to female transgender	44.4 (1274/2870)	38.1 (751/1973)	58.3 (523/897)
Race or ethnicity:			
White, non-Hispanic	69.5 (2013/2896)	71.2 (1421/1996)	65.8 (592/900)
Hispanic	16.2 (468/2896)	17.0 (339/1996)	14.3 (129/900)
Black or African American, non-Hispanic	10.5 (305/2896)	8.7 (174/1996)	14.6 (131/900)
Other, non-Hispanic	3.8 (110/2896)	3.1 (62/1996)	5.3 (48/900)
Detox in past year	—	47.3 (950/2007)	NA
Incarceration in past year	—	27.1 (460/1695)	NA
Lifetime history of overdose	—	54.0 (976/1808)	NA
Received naloxone at last overdose	—	60.0 (503/838)	NA
Overdose witnessed ever	73.6 (2036/2767)	80.8 (1571/1944)	56.5 (465/823)
Reported at least one overdose rescue	7.3 (212/2912)	9.2 (184/2007)	3.1 (28/905)

NA=not available.

Denominators less than total number for each group are due to missing information.

*Geographically distinct cities and towns.

†Enrollees who self reported active substance misuse, currently engaged in treatment or in recovery at enrollment.

Table 3| Overdose rescue attempts reported by bystanders trained in the overdose education and nasal naloxone distribution program in 19 Massachusetts communities*, 2006-09

Variables	% (No/No in group)		
	All enrollees (n=327)	Users† (n=286)	Non-users (n=41)
Status of person who overdosed:			
Friend	69 (216/313)	72 (200/276)	43 (16/37)
Partner or family	16 (49/313)	12 (34/276)	41 (15/37)
Stranger	10 (32/313)	9 (26/276)	16 (6/37)
Self	5 (16/313)	6 (16/276)	0 (0/37)
Overdose setting:			
Private	78 (249/317)	80 (221/277)	70 (28/40)
Public	22 (68/317)	20 (56/277)	30 (12/40)
No of doses used:			
1	48 (149/312)	48 (129/272)	50 (20/40)
2	48 (150/312)	48 (130/272)	50 (20/40)
≥3	4 (13/312)	5 (13/272)	0 (0/40)
Naloxone successful	98 (150/153)	98 (130/133)	100 (20/20)
911 called or emergency personnel present	33 (106/326)	26 (75/285)	76 (31/41)
Rescue breathing performed	38 (123/327)	37 (105/286)	44 (18/41)
Stayed with victim until alert and awake or help arrived	89 (287/321)	90 (253/280)	83 (34/41)

Denominators less than total number for each group are due to missing information.

*Geographically distinct cities and towns.

†Enrollees who self reported active substance use, currently engaged in treatment or in recovery at enrollment.

Table 4| Models of overdose education and nasal naloxone distribution implementation and unintentional opioid related overdose death rates in 19 communities* in Massachusetts, 2002-09

Cumulative enrollments per 100 000 population	Rate ratio	Adjusted rate ratio† (95% CI)	P value
Absolute model:			
No implementation	Reference	Reference	
Low implementation: 1-100 enrollments	0.93	0.73 (0.57 to 0.91)	<0.01
High implementation: >100 enrollments	0.82	0.54 (0.39 to 0.76)	<0.01
Relative model:			
No implementation	Reference	Reference	
Low implementation: <median	0.85	0.71 (0.57 to 0.90)	<0.01
High implementation: >median	1.00	0.78 (0.60 to 1.01)	0.06

*Geographically distinct cities and towns.

†Adjusted for city/town population rates of age under 18, male, race or ethnicity (Hispanic, white, black, other), below poverty level, medically supervised inpatient withdrawal treatment, methadone treatment, Bureau of Substance Abuse Services funded buprenorphine treatment, prescriptions to doctor shoppers (individuals with schedule II opioid prescriptions from ≥4 prescribers and filled prescriptions at ≥4 pharmacies in 12 month period), and year.

Table 5| **Models of overdose education and nasal naloxone distribution implementation and opioid overdose related acute care hospital utilizations in 19 communities* in Massachusetts, 2002-09**

Cumulative enrollments per 100 000 population	Rate ratio	Adjusted rate ratio† (95% CI)	P value
Absolute model:			
No implementation	Reference	Reference	
Low implementation: 1-100 enrollments	1.00	0.93 (0.80 to 1.08)	0.4
High implementation: >100 enrollments	1.06	0.92 (0.75 to 1.13)	0.4
Relative model:			
No implementation	Reference	Reference	
Low implementation: <median	0.96	0.90 (0.76 to 1.07)	0.2
High implementation: >median	1.10	1.00 (0.86 to 1.16)	1.0

*Geographically distinct cities and towns.

†Adjusted for city/town population rates of age under 18, male, race or ethnicity (Hispanic, white, black, other), below poverty level, medically supervised inpatient withdrawal treatment, methadone treatment, Bureau of Substance Abuse Services funded buprenorphine treatment, prescriptions to doctor shoppers (individuals with schedule II opioid prescriptions from ≥4 prescribers and filled prescriptions at ≥4 pharmacies in 12 month period), and year.
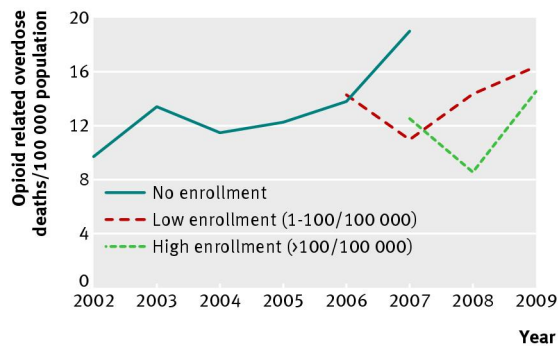
Figures

Fig 1 Unadjusted unintentional opioid related overdose death rates in 19 communities with no, low, and high enrollment in overdose education and nasal naloxone distribution program in Massachusetts, 2002-09
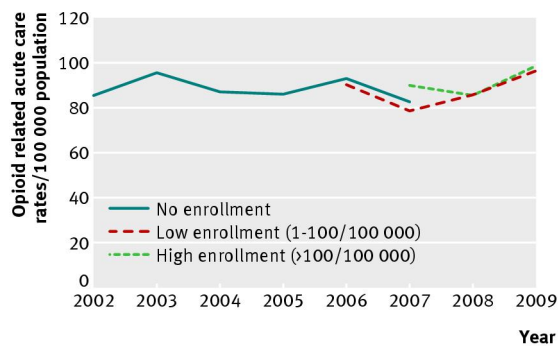

Fig 2 Unadjusted opioid related acute care hospital utilization rates in 19 communities with no, low, and high enrollment in overdose education and nasal naloxone distribution program in Massachusetts, 2002-09