ORIGINAL ARTICLE

Community-Based Cluster-Randomized Trial to Reduce Opioid Overdose Deaths

The HEALing Communities Study Consortium

ABSTRACT

BACKGROUND

Evidence-based practices for reducing opioid-related overdose deaths include overdose education and naloxone distribution, the use of medications for the treatment of opioid use disorder, and prescription opioid safety. Data are needed on the effectiveness of a community-engaged intervention to reduce opioid-related overdose deaths through enhanced uptake of these practices.

METHODS

In this community-level, cluster-randomized trial, we randomly assigned 67 communities in Kentucky, Massachusetts, New York, and Ohio to receive the intervention (34 communities) or a wait-list control (33 communities), stratified according to state. The trial was conducted within the context of both the coronavirus disease 2019 (Covid-19) pandemic and a national surge in the number of fentanyl-related overdose deaths. The trial groups were balanced within states according to urban or rural classification, previous overdose rate, and community population. The primary outcome was the number of opioid-related overdose deaths among community adults.

RESULTS

During the comparison period from July 2021 through June 2022, the population-averaged rates of opioid-related overdose deaths were similar in the intervention group and the control group (47.2 deaths per 100,000 population vs. 51.7 per 100,000 population), for an adjusted rate ratio of 0.91 (95% confidence interval, 0.76 to 1.09; P=0.30). The effect of the intervention on the rate of opioid-related overdose deaths did not differ appreciably according to state, urban or rural category, age, sex, or race or ethnic group. Intervention communities implemented 615 evidence-based practice strategies from the 806 strategies selected by communities (254 involving overdose education and naloxone distribution, 256 involving the use of medications for opioid use disorder, and 105 involving prescription opioid safety). Of these evidence-based practice strategies, only 235 (38%) had been initiated by the start of the comparison year.

CONCLUSIONS

In this 12-month multimodal intervention trial involving community coalitions in the deployment of evidence-based practices to reduce opioid overdose deaths, death rates were similar in the intervention group and the control group in the context of the Covid-19 pandemic and the fentanyl-related overdose epidemic. (Funded by the National Institutes of Health; HCS ClinicalTrials.gov number, NCT04111939.)

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A Quick Take is available at NEJM.org

Rates of opioid-related overdose deaths have been a rising scourge in the United States, with an increase in the annual number of deaths from 8050 in 1999[1] to 82,136 in 2022.[2] This increase was initially attributed to excessive opioid prescribing and more recently to the expansion of fentanyl in the illicit drug supply.[3] Fentanyl has become the primary illicit opioid and has contaminated stimulants[4] and counterfeit pills,[5] along with escalating the rate of opioid-related overdose deaths disproportionately among Black and Indigenous populations.[6,7]

In 2016, the U.S. Surgeon General urged medical professionals to address the opioid crisis through advocacy, stigma reduction, uptake of treatment for opioid use disorder, and safer opioid prescribing.[8] The National Academy of Medicine echoed this recommendation in 2017.[9] Both reports highlighted the value of evidence-based practices to prevent or reverse opioid overdoses. These practices include education regarding overdose prevention and naloxone distribution,[10,11] the use of medications (including methadone and buprenorphine) for the treatment of opioid use disorder,[12,13] and safer opioid prescribing, dispensing, and disposal practices (i.e., prescription opioid safety).[14]

Despite efforts to advance evidence-based practices in the United States,[15] patient-level and organizational barriers such as stigma[16] and regulations[9] impede care delivery,[9,17] transportation options,[18] prescriber access,[19] and naloxone availability.[20] In the United States, fewer than 1 in 5 persons with opioid use disorder received medications for treatment in 2021,[21] with even lower rates among Black persons.[22] Overdose education at the community level and the availability of naloxone distribution are inadequate to achieve a substantial reduction in opioid-related overdose deaths, according to simulation models.[23]

To address these barriers, the National Institutes of Health launched the HEALing (Helping to End Addiction Long-term Initiative) Communities Study (HCS), a large, multistate implementation-science trial focused on substance use.[24] The HCS research consortium designed the community-engaged, data-driven Communities That HEAL (CTH) intervention to rapidly scale up strategies to increase access to evidence-based practices and conduct communication campaigns in highly affected communities in Kentucky, Massachusetts, New York, and Ohio, with the primary goal of reducing the rate of opioid-related overdose deaths.[25]

Methods

Trial Design and Oversight

The HCS was a multisite, community-level, cluster-randomized, controlled trial to evaluate the CTH intervention in reducing the rate of opioid-related overdose deaths in highly affected communities.[25] The trial was grounded in the Reach, Effectiveness, Adoption, Implementation, and Maintenance (RE-AIM) and the Practical, Robust Implementation and Sustainability Model (PRISM) implementation-science framework.[26]

The trial protocol (available with the full text of this article at NEJM.org) was approved by Advarra, a company providing research review services that served as the single institutional review board for the trial. A waiver of consent and full waiver of Health Insurance Portability and Accountability Act (HIPAA) authorization were granted for secondary data analysis. The data and safety monitoring board, chartered by the National Institute on Drug Abuse, monitored the trial. Data that are reported in this trial are protected by multiple data-use agreements among researchers and agencies providing the data.

The authors vouch for the completeness and accuracy of the data and for the fidelity of the trial to the protocol. Details regarding the authors' roles in manuscript preparation are provided in Figure S1 in the Supplementary Appendix, available at NEJM.org.

Trial Population

All the participating communities (the unit of analysis) had a high baseline rate of opioid-related overdose deaths (≥25 per 100,000 adults); at least 30% of the communities were rural. The demographic characteristics of the trial populations were similar to those in the overall U.S. populations that have been severely affected by fatal opioid overdoses (Fig. S2).

Trial Procedures, Intervention, and Randomization

The CTH intervention was adapted from the evidence-based Communities That Care approach that used a five-phase process to support communities in selecting and implementing evidence-based practices to prevent adolescent substance use.[27] The CTH intervention used a similar phased-planning process with community coalitions that included local residents who had involvement in the crisis of opioid use disorder through their vocation or personal experience.[28] Coalitions assessed the local effect of opioid overdose using data to understand gaps and resources.[29] They implemented communication campaigns promoting opioid overdose education and naloxone distribution, the use of medications for opioid use disorder, and messages to reduce stigma through print, digital, radio, outdoor, and social media channels.[30] Funds were allocated to the HCS intervention communities to implement strategies for evidence-based practices and communication campaigns, with an average allocation per intervention community of $672,000 in New York, $922,500 in Ohio, $1.69 million in Kentucky, and $1.72 million in Massachusetts.

The HCS investigators have previously described the implementation-science framework[26] and the CTH intervention, along with strategies and implementation resources,[31] community-engaged processes to select and promote adoption and sustainability of evidence-based practices,[29] communication campaigns to drive demand and reduce stigma,[30] and community dashboards to support data-driven strategy selection.[32] A strategy for evidence-based practices was considered to have been implemented if at least one service had been delivered. The number of persons who had been exposed to each strategy was not uniformly assessed. Thus, the pragmatic definition threshold for implementation was the provision of a single service.

We used a covariate-constrained randomization procedure,[33] stratified according to state. Within each state, the intervention and control groups were balanced according to urban or rural classification, rate of opioid-related overdose deaths, and population.[25]

TIMELINE

The intervention was delivered from January 2020 through June 2022 and later to the previous control communities from July 2022 through December 2023 (Fig. S3). Most implementation of evidence-based practices in the intervention communities occurred from September 2020 through June 2022, except for some early overdose education and naloxone distribution strategies in response to orders for early release of inmates from detention centers related to the coronavirus 2019 disease (Covid-19) pandemic. The comparison period between intervention and control communities was the 12-month period from the beginning of July 2021 through the end of June 2022.[28]

OUTCOMES

The primary outcome was the number of opioid overdose deaths among community adults, as determined from death certificates with drug overdose as an underlying cause of death (*International Classification of Diseases, 10th Revision* [ICD-10] codes X40 to X44, X60 to X64, X85, and Y10 to Y14) due to opioids (contributing cause of death, ICD-10 codes, T40.0 to T40.4 and T40.6). In Kentucky, additional death-investigation records determined opioid involvement if specific drugs were absent from death certificates.[34] Deaths were attributed to individual communities on the basis of the residence address on the death certificate. A post hoc secondary analysis evaluated the change in rates from 2019 through the comparison period as the outcome.

ADVERSE EVENTS

We used the mean rate of emergency medical service runs for a suspected opioid overdose per 1000 adults to assess potential adverse events and serious adverse events in the community. Adverse events and serious adverse events were reported if a community rate in a single month increased by more than 3 standard deviations above the moving average of the previous 3 months for adverse events or by more than 4 standard deviations for serious adverse events. The number of emergency medical service runs for a suspected opioid overdose was a surrogate measure for opioid-related overdose deaths because of the much shorter lag-time availability for data regarding such runs as compared with deaths (1 to 3 months vs. 6 to 11 months).

STATISTICAL ANALYSIS

We determined that the inclusion of 67 communities would provide the trial with 99% power to detect a prespecified 40% reduction in the rate of opioid-related overdose deaths in the intervention group as compared with the control group and 83% power to detect a 20% reduction in the

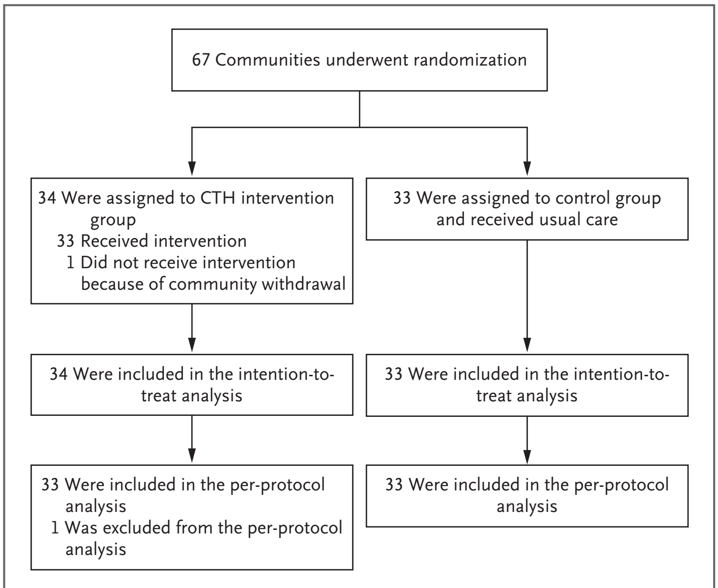

Figure 1. Enrollment and Randomization.

Shown are the randomization procedures and analyses that were performed in the 67 communities that participated in the HEALing Communities Study (HCS) in Kentucky, Massachusetts, New York, and Ohio. The HCS research consortium designed the Communities That HEAL (CTH) intervention to rapidly scale up strategies to reduce the rate of opioid-related overdose deaths. One intervention community was not included in the per-protocol analysis because the community withdrew before the initiation of the intervention.

overdose death rate. We performed analyses using the intention-to-treat principle for the 67 randomized communities. There were no missing data for these analyses. A negative binomial regression analysis modeled the population-averaged rate of opioid-related overdose deaths with the natural log of the adult community population as the offset, after adjustment for state, urban or rural classification, and community-level baseline rates.[35] Small sample-adjusted empirical estimates of standard error were used to ensure valid inference.[36] The model accounted for clustering by means of the overdispersion parameter; the estimated positive value (i.e., variance exceeding mean) indicated that the negative binomial model was appropriate.

In prespecified exploratory analyses, the primary model was extended to assess the potential interaction of trial group and five variables: state, urban or rural category, age (categorical), sex, and race or ethnic group. We applied multiple-testing adjustments according to the Benjamini–Hochberg procedure[37] (using sequential modified Bonferroni correction for multiple hypothesis testing) only to the P values from the five effect-modification tests. We report rate ratio estimates to compare the two groups of communities for each level of the given categorical variables, along with 95% confidence intervals adjusted by a Bonferroni correction on the basis of the number of levels.

We performed a secondary per-protocol analysis with the exclusion of one intervention community that withdrew before the initiation of the intervention. The primary test was two-sided, with a P value of less than 0.05 indicating statistical significance.

A series of post hoc analyses (Table S1) included four sensitivity analyses in which we fit a modified Poisson regression model, which assumed no overdispersion; used log transformation for the baseline rate of opioid-related overdose deaths, which excluded one community with no deaths at baseline; included an interaction between state and urban or rural category; included an interaction between the intervention group and the state, which generated a rate ratio averaged across states; and evaluated combinations of the five variables as listed above. We assessed the goodness of fit for both the negative binomial and Poisson models and determined that the negative binomial provided a better fit than the Poisson model on the basis of plots of deviance residuals (Fig. S4), various fit statistics (Table S2), and the positive dispersion parameter. All the analyses were performed with the use of SAS software, version 9.4 (SAS Institute). The results of secondary and exploratory analyses that were not part of a hierarchical statistical plan and that controlled for multiple comparisons are reported as point estimates with 95% confidence intervals, from which causal inferences should not be made.

RESULTS

BASELINE CHARACTERISTICS

The 67 communities (adult population, 8.2 million) were randomly assigned to either the intervention group (34 communities, including 15 rural) or the control group (33 communities, including 14 rural) (Fig. 1 and Fig. S5). The designated communities included 48 counties, 14 municipalities (11 in Massachusetts and 3 in New York), and rural clusters of municipalities (5 in Massachusetts). The mean (±SD) baseline rate of opioid-related overdose deaths was similar in the intervention group and the control group (38.2±22.8 and 37.1±20.3 per 100,000 population, respectively). Baseline community characteristics are shown in Table 1.[38,39]

IMPLEMENTATION OF EVIDENCE-BASED PRACTICES

Intervention communities implemented 615 evidence-based practice strategies (254 involving overdose education and naloxone distribution, 256 involving the use of medications for opioid use disorder, and 105 involving prescription opioid safety). However, only 235 of the 615 strategies (38%) were implemented before the comparison period: 43% involving overdose education and naloxone distribution, 36% involving the use of medications for opioid use disorder, and 32% involving prescription opioid safety. Details regarding the implementation of these strategies are provided in Tables S3, S4, and S5.

RATES OF OPIOID OVERDOSE DEATHS

Unadjusted means and rate ratios for the number of opioid-related overdose deaths during the 12-month comparison period are reported according to trial group, state, urban or rural category, age, sex, and race or ethnic group (Table 2).[40] The overall unadjusted rate ratios of opioid-related overdose deaths comparing the intervention group with the control group were 0.94 (on the basis of the mean unadjusted rates across communities) and 0.82 (on the basis of the sum of unadjusted rates across communities). In the primary adjusted analyses, the rate of opioid-related overdose deaths was 47.2 per 100,000 population for the intervention communities and 51.7 per 100,000 population for the control communities (rate ratio, 0.91; 95% confidence interval [CI], 0.76 to 1.09; P=0.30) (Table 3). The results of the per-protocol analysis were similar to those in the primary analysis (Table 3). There was no evidence of effect modification according to state, urban or rural category, age, sex, or race or ethnic group (Table 4), although there was substantial variability among states and among urban and rural locations.

ADVERSE EVENTS

The risks of adverse events and serious adverse events (as defined according to the number of opioid-related emergency medical service runs) were similar in the two groups (Table S6). None of the adverse events or serious adverse events were attributed to the trial intervention.

PROTOCOL DEVIATIONS AND NONCOMPLIANCE REPORTS

Five protocol deviations were reported with respect to consent procedures. One noncompliance report was related to a lack communication with the institutional review board regarding revisions to the trial protocol (Fig. S6).

DISCUSSION

The HCS was a large implementation-science trial focused on substance use involving 67 communities with high rates of opioid-related overdose deaths in four states. During the comparison year (July 2021 through June 2022) across communities, 4517 deaths were linked to opioid overdoses. Despite the breadth and depth of the intervention, the risk of opioid-related overdose death was similar in the intervention group and the control group. Numerous factors may have tempered the effect of the intervention. Of these factors, three warrant discussion: the duration and intensity of the implementation, the Covid-19 pandemic, and the evolving illicit drug market.

First, the evidence-based practices were addressed by a complex array of strategies for high-risk populations in health care, behavioral health, and criminal legal sectors. After the strategy selection process, only 10 months preceded the comparison period to establish agency partnerships and implement evidence-based practices.[28] The time frame was insufficient to initiate many strategies for evidence-based practices, which often required recruiting new staff from an increasingly scarce health care workforce, changing clinical practice workflows, or developing new interagency collaborations to introduce services (e.g., in criminal legal settings). Ultimately, 615 strategies were implemented, which suggests the effectiveness of the CTH intervention in mobilizing communities to pursue the adoption of evidence-based practices. However, greater penetrance of the practices through continuous quality improvement and longer time horizons may be needed to observe the full effect of the CTH intervention on opioid-related overdose deaths.[41]

Second, the intervention launch (in January 2020) occurred 2 months before the Covid-19 shutdown, which severely disrupted systems targeted by the CTH intervention. Through a protocol amendment, 6 months were added for imple-

Table 1. Characteristics of the 67 Communities at Baseline.*

Variable	Intervention Communities				Control Communities				Rate Ratio
	Community (N=67)	Opioid-Related Overdose Deaths	Population†	Death Rate	Community (N=67)	Opioid-Related Overdose Deaths	Population†	Death Rate	
	no. (%)	*no.*		*no./100,000 population*	*no. (%)*	*no.*		*no./100,000 population*	
All communities	34 (50.7)	1771	4,439,170	39.9	33 (49.3)	1546	3,772,336	41.0	0.97
Opioid-related overdose deaths									
Mean no.	—	—	—	38.2±22.8	—	—	—	37.1±20.3	—
Median no. (IQR)	—	—	—	35.2 (21.6–49.3)	—	—	—	32.7 (23.6– 48.6)	—
State									
Kentucky	8 (23.5)	260	617,841	42.1	8 (24.2)	361	815,764	44.3	0.95
Massachusetts	8 (23.5)	172	359,314	47.9	8 (24.2)	201	356,545	56.4	0.85
New York	8 (23.5)	256	1,101,497	23.2	8 (24.2)	318	976,069	32.6	0.71
Ohio	10 (29.4)	1083	2,360,518	45.9	9 (27.3)	666	1,623,958	41.0	1.12
Urban or rural category									
Urban	19 (55.9)	1538	3,793,353	40.5	19 (57.6)	1377	3,242,663	42.5	0.95
Rural	15 (44.1)	233	645,817	36.1	14 (42.4)	169	529,673	31.9	1.13
Age group — yr									
18 to 34	—	531	1,334,880	39.8	—	508	1,178,210	43.1	0.92
35 to 54	—	848	1,353,341	62.7	—	751	1,180,392	63.6	0.98
≥55	—	392	1,750,949	22.4	—	287	1,413,734	20.3	1.10
Sex									
Male	—	1235	2,133,827	57.9	—	1071	1,825,776	58.7	0.99
Female	—	536	2,305,343	23.3	—	475	1,946,560	24.4	0.95

Race or ethnic group‡									
Non-Hispanic White	—	1374	3,229,233	42.5	—	1119	2,750,369	40.7	1.05
Non-Hispanic Black	—	267	728,037	36.7	—	278	545,357	51.0	0.72
Hispanic	—	115	281,329	40.9	—	130	322,654	40.3	1.01
Non-Hispanic other	—	12	200,571	6.0	—	17	153,956	11.0	0.54
Missing data	—	3			—	2			

* Plus–minus values are means ±SD. Percentages may not total 100 due to rounding. IQR denotes interquartile range.
† For communities that represent counties (48 of 67), population estimates are from 2020 Bridged-Race Population Estimates.[39] For communities that represent units smaller than counties (19 of 67), population estimates are from the 2017–2021 American Community Survey 5-Year Estimates.[40]
‡ Race or ethnic group was reported on death certificates.

mentation, but the initiation of activities of the organizations was still delayed. Hence, the pandemic reduced the capacity of communities to implement the CTH intervention, which mitigated the potential for the intervention to affect the rate of opioid-related overdose deaths.

Third, the change in the illicit drug market may have reduced the effectiveness of the intervention, because fentanyl became a more prevalent opioid and a more commonly used adulterant in stimulants[4] and counterfeit pills.[5] Both fentanyl and, increasingly, xylazine[42] posed new challenges for opioid-overdose treatment. We do not know whether surges in fentanyl use over time were similar across communities.

The embrace of evidence-based practices by coalitions in the intervention communities varied considerably in part because of competing challenges posed by the Covid-19 pandemic, the fentanyl epidemic, and continuing stigma related to drug use — all of which affected willingness and capacity to respond to the opioid crisis. The CTH intervention had a major effect on the implementation of evidence-based practices (615 of 806 that were selected) and communication campaigns (with 165 implemented). Failure to observe significant reductions in opioid-related overdose deaths may have resulted from the temporal lags between organizational implementation and the servicing of a sufficiently large number of affected persons. In retrospect, the prespecified 40% reduction in opioid-related overdose deaths was clearly ambitious. The trial may have been underpowered to detect substantially smaller yet clinically meaningful differences.

The trial has several strengths. The coalitions used timely data to inform the selection of many strategies for evidence-based practices and communication. Heterogeneous coalitions, including members with lived experience who were working with university and state public health partners, enhanced the decision-making process and established partnerships for future sustainability. The randomized, controlled trial design involving 67 communities that were balanced with respect to key covariates addressed threats to internal validity. Finally, coalitions created a sense of urgency and developed partnerships among community agencies, persons with lived experience, public health practitioners, and government officials to address the opioid crisis.

Several trial limitations are noteworthy. First,

Table 2. Unadjusted Rate Ratio of Opioid-Related Overdose Deaths (Intention-to-Treat Population).*

Variable	Intervention Communities		Control Communities		Unadjusted Rate Ratio
	Opioid-Related Overdose Deaths	Population	Opioid-Related Overdose Deaths	Population	
	number of persons				
All communities	65.3±98.1	130,563.8±200,088.0	69.6±143.8	114,313.2±201,417.3	0.94
State					
Kentucky	48.9±46.5	77,230.1±80,938.9	76.1±168.7	101,970.5±202,045.3	1.11
Massachusetts	25.1±22.2	44,914.3±26,559.3	30.1±24.7	44,568.1±33,628.8	0.74
New York	59.0±73.9	137,687.1±140,779.9	67.9±74.6	122,008.6±106,012.1	0.73
Ohio	115.6±156.3	236,051.8±322,922.0	100.4±223.0	180,439.8±325,173.2	1.24
Urban or rural category					
Urban	100.2±120.1	199,650.2±248,385.2	106.8±182.1	170,666.5±252,614.9	0.96
Rural	21.1±19.4	43,054.5±19,075.4	19.1±14.8	37,833.8±23,733.0	0.92
Age group — yr					
18 to 34	17.6±25.6	39,261.2±60,440.2	19.5±42.1	35,703.3±69,802.6	0.88
35 to 54	32.4±48.8	39,804.1±60,321.8	33.7±70.3	35,769.5±65,163.6	0.97
≥55	15.3±24.7	51,498.5±79,908.4	16.4±32.3	42,840.4±67,485.8	0.97
Sex					
Male	44.9±68.2	62,759.6±94,370.9	48.5±98.4	55,326.5±96,853.5	0.89
Female	20.4±30.1	67,804.2±105,743.9	21.1±45.6	58,986.7±104,579.4	1.08
Race or ethnic group					
Non-Hispanic White	46.6±61.6	94,977.4±128,763.1	46.6±91.2	83,344.5±135,601.7	0.97
Non-Hispanic Black	13.6±30.6	21,412.9±55,089.6	16.2±46.9	16,526.0±45,296.8	0.96
Hispanic	4.0±8.0	8,274.4±13,482.1	5.4±10.8	9,777.4±17,743.5	0.77
Non-Hispanic other	0.9±2.2	5,899.1±9,757.0	1.2±2.9	4,665.3±11,990.9	0.79
Missing data	0.3±0.8		0.4±0.9		

* Plus–minus values are means ±SD. Listed are data for adults (≥18 years of age) during the comparison period from July 1, 2021, to June 30, 2022. For communities that represent counties (48 of 67), population information is drawn from 2020 Bridged-Race Population Estimates.[39] For communities that represent units smaller than counties (19 of 67), population information is drawn from 2017–2021 American Community Survey 5-Year Estimates.[40]

Table 3. Adjusted Rate of Opioid-Related Overdose Deaths, According to Population.*

Population	Adjusted Rate in Intervention Communities (95% CI)	Adjusted Rate in Control Communities (95% CI)	Adjusted Rate Ratio (95% CI)	P Value†
	no./100,000 population			
Intention-to-treat analysis	47.2 (41.8–53.2)	51.7 (44.9–59.6)	0.91 (0.76–1.09)	0.30
Per-protocol analysis	47.2 (41.8–53.3)	51.6 (44.8–59.4)	0.91 (0.77–1.09)	—

* Listed are results obtained during the comparison period from July 1, 2021 through June 30, 2022. Data were analyzed by means of a negative binomial model after adjustment for trial group, state (Kentucky, Massachusetts, New York, and Ohio), urban or rural category, and baseline rate of opioid-related overdose deaths. The natural log of the community population size during the comparison period is used as an offset.

† P values are reported only for the primary analysis and for additional prespecified analyses that controlled for multiple testing.

Table 4. Adjusted Rate of Opioid-Related Overdose Deaths (Intention-to-Treat Population).*

Variable	Adjusted Rate in Intervention Communities (95% CI)	Adjusted Rate in Control Communities (95% CI)	Adjusted Rate Ratio (95% CI)
	no./100,000 population		
State			
Kentucky	59.8 (44.5–80.4)	59.3 (35.5–99.2)	1.01 (0.56–1.81)
Massachusetts	45.0 (30.7–65.9)	52.2 (38.0–71.8)	0.86 (0.54–1.37)
New York	46.4 (32.1–67.0)	53.1 (41.7–67.7)	0.87 (0.56–1.35)
Ohio	39.3 (31.7–48.7)	43.0 (28.9–64.1)	0.91 (0.58–1.44)
Urban or rural category			
Urban	48.2 (41.5–55.9)	50.3 (41.6–60.9)	0.96 (0.76–1.21)
Rural	45.1 (35.3–57.7)	54.4 (41.4–71.5)	0.83 (0.57–1.20)
Age — yr			
18 to 34	46.2 (39.8–53.5)	51.3 (42.4–62.1)	0.90 (0.72–1.13)
35 to 54	69.9 (58.2–83.9)	76.6 (64.8–90.5)	0.91 (0.73–1.15)
≥55	33.6 (27.8–40.7)	39.3 (28.9–53.6)	0.86 (0.59–1.23)
Sex			
Male	60.6 (50.6–72.6)	69.2 (58.4–82.1)	0.88 (0.71–1.08)
Female	34.1 (29.0–40.0)	37.2 (30.2–45.8)	0.91 (0.71–1.18)
Race or ethnic group			
Non-Hispanic White	45.4 (36.6–56.3)	47.6 (38.0–59.5)	0.95 (0.72–1.26)
Non-Hispanic Black	70.3 (52.4–94.2)	77.1 (54.9–108.4)	0.91 (0.59–1.40)
Hispanic	39.3 (24.4–63.3)	46.4 (31.6–68.0)	0.85 (0.46–1.57)
Non-Hispanic other	16.5 (7.5–36.4)	28.2 (13.6–58.7)	0.59 (0.20–1.68)

* Listed are results obtained during the comparison period from July 1, 2021 through June 30, 2022. A separate negative binomial model was fit for each test of effect modification. Each model included the fixed effects of trial group, state, urban or rural category, baseline opioid-related overdose death rate, stratification variable (age, sex, and race or ethnic group), and a two-way interaction between the trial group and the stratification variable.

despite randomization, differences among states may have played a role in observed outcomes. For example, the number of residents in HCS communities in the state with the lowest population (Massachusetts, with 715,859 residents) was less than 20% of that in the state with the highest population (Ohio, with 3,984,476 residents). In addition, the steep rise in opioid-related overdose deaths during the Covid-19 pandemic was not uniform across states. For example, from January 2020 through June 2022, Kentucky had an increase in deaths of 77% as compared with an increase of 15% in Massachusetts.[2] These differences led to variation in the absolute number of persons who could benefit from the allocated trial resources. It is possible that secular trends and contamination by the inadvertent exposure of control communities to evidence-based practice strategies may have attenuated the effect of the CTH intervention. For example, control communities could access non-HCS funds to address the opioid epidemic. These funds became more available in response to increases in opioid-related overdose deaths during the Covid-19 pandemic and may have resulted in activities that could have masked an intervention effect. Also, adults in control communities that were proximal to intervention communities may have been exposed to CTH evidence-based practices and communication campaigns. Another limitation is that the HCS did not consistently assess the number of persons who were affected by the strategies that were implemented in the intervention communities.

HCS investigators examined the potential of the community-engaged, data-driven CTH intervention to reduce the rate of opioid-related overdose deaths in highly affected communities. Intervention communities implemented hundreds of strategies to expand opioid overdose education and naloxone distribution, the use of medications for opioid use disorder, and safety measures for prescription opioid use, as well as communication campaigns to support these efforts. Although there were no significant between-group differences in the rate of opioid-related overdose deaths, the trial showed that the CTH community-engaged intervention, with its leveraging of community coalitions and a data-driven approach, can bring about meaningful progress in implementing evidence-based practices.

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REFERENCES

1. National Institute on Drug Abuse. Drug overdose deaths: facts and figures. January 20, 2022 (https://nida.nih.gov/research-topics/trends-statistics/overdose-death-rates).
2. Ahmad FB, Cisewski JA, Rossen LM, Sutton P. Provisional drug overdose death counts. Hyattsville, MD: National Center for Health Statistics, 2024 (https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm).
3. O'Donnell JK, Gladden RM, Seth P. Trends in deaths involving heroin and synthetic opioids excluding methadone, and law enforcement drug product reports, by Census region — United States, 2006–2015. MMWR Morb Mortal Wkly Rep 2017;66:897-903.
4. Wagner KD, Fiuty P, Page K, et al. Prevalence of fentanyl in methamphetamine and cocaine samples collected by community-based drug checking services. Drug Alcohol Depend 2023;252:110985.
5. O'Donnell J, Tanz LJ, Miller KD, et al. Drug overdose deaths with evidence of counterfeit pill use — United States, July 2019–December 2021. MMWR Morb Mortal Wkly Rep 2023;72:949-56.
6. Han B, Einstein EB, Jones CM, Cotto J, Compton WM, Volkow ND. Racial and ethnic disparities in drug overdose deaths in the US during the COVID-19 pandemic. JAMA Netw Open 2022;5(9):e2232314.
7. Friedman JR, Hansen H. Evaluation of increases in drug overdose mortality rates in the US by race and ethnicity before and during the COVID-19 pandemic. JAMA Psychiatry 2022;79:379-81.
8. Murthy VH. Ending the opioid epidemic — a call to action. N Engl J Med 2016;375:2413-5.
9. National Academies of Sciences, Engineering, and Medicine. Medications for opioid use disorder save lives. Washington, DC: National Academies Press, 2019 (http://www.ncbi.nlm.nih.gov/books/NBK538936/).
10. Clark AK, Wilder CM, Winstanley EL. A systematic review of community opioid overdose prevention and naloxone distribution programs. J Addict Med 2014;8:153-63.
11. Giglio RE, Li G, DiMaggio CJ. Effectiveness of bystander naloxone administration and overdose education programs: a meta-analysis. Inj Epidemiol 2015;2:10.
12. Larochelle MR, Bernson D, Land T, et al. Medication for opioid use disorder after nonfatal opioid overdose and association with mortality: a cohort study. Ann Intern Med 2018;169:137-45.
13. Sordo L, Barrio G, Bravo MJ, et al. Mortality risk during and after opioid substitution treatment: systematic review and meta-analysis of cohort studies. BMJ 2017;357:j1550.
14. Dowell D, Ragan KR, Jones CM, Baldwin GT, Chou R. CDC clinical practice guideline for prescribing opioids for pain — United States, 2022. MMWR Recomm Rep 2022;71(3):1-95.
15. Biden-Harris administration announces new actions and funding to address the overdose epidemic and support recovery. Fact sheet. Washington, DC: White House, September 23, 2022 (https://www.whitehouse.gov/briefing-room/statements-releases/2022/09/23/fact-sheet-biden-harris-administration-announces-new-actions-and-funding-to-address-the-overdose-epidemic-and-support-recovery/).
16. Kennedy-Hendricks A, Barry CL, Gollust SE, Ensminger ME, Chisolm MS, McGinty EE. Social stigma toward persons with prescription opioid use disorder: associations with public support for punitive and public health-oriented policies. Psychiatr Serv 2017;68:462-9.
17. Madras BK, Ahmad NJ, Wen J, Sharfstein JS. Improving access to evidence-based medical treatment for opioid use disorder: strategies to address key barriers within the treatment system. NAM Perspect 2020 April 27 (Epub ahead of print).
18. Pullen E, Oser C. Barriers to substance abuse treatment in rural and urban communities: counselor perspectives. Subst Use Misuse 2014;49:891-901.
19. McBain RK, Dick A, Sorbero M, Stein BD. Growth and distribution of buprenorphine-waivered providers in the United States, 2007-2017. Ann Intern Med 2020;172:504-6.
20. Peet ED, Powell D, Pacula RL. Trends in out-of-pocket costs for naloxone by drug brand and payer in the US, 2010-2018. JAMA Health Forum 2022;3(8):e222663.
21. Substance Abuse and Mental Health Services Administration. Key substance use and mental health indicators in the United States: results from the 2022 National Survey on Drug Use and Health (HHS publication no. PEP23-07-01-006, NSDUH series H-58). 2023 (https://www.samhsa.gov/data/report/2022-nsduh-annual-national-report).
22. Barnett ML, Meara E, Lewinson T, et al. Racial inequality in receipt of medications for opioid use disorder. N Engl J Med 2023;388:1779-89.
23. Nataraj N, Rikard SM, Zhang K, et al. Public health interventions and overdose-related outcomes among persons with opioid use disorder. JAMA Netw Open 2024;7(4):e244617.
24. Chandler RK, Villani J, Clarke T, McCance-Katz EF, Volkow ND. Addressing opioid overdose deaths: the vision for the HEALing Communities Study. Drug Alcohol Depend 2020;217:108329.
25. HEALing Communities Study Consortium. The HEALing (Helping to End Addiction Long-term) Communities Study: protocol for a cluster randomized trial at the community level to reduce opioid overdose deaths through implementation of an integrated set of evidence-based practices. Drug Alcohol Depend 2020;217:108335.
26. Glasgow RE, Harden SM, Gaglio B, et al. RE-AIM planning and evaluation framework: adapting to new science and practice with a 20-year review. Front Public Health 2019;7:64.
27. Hawkins JD, Oesterle S, Brown EC, et al. Results of a type 2 translational research trial to prevent adolescent drug use and delinquency: a test of Communities That Care. Arch Pediatr Adolesc Med 2009;163:789-98.
28. Young AM, Brown JL, Hunt T, et al. Protocol for community-driven selection of strategies to implement evidence-based practices to reduce opioid overdoses in the HEALing Communities Study: a trial to evaluate a community-engaged intervention in Kentucky, Massachusetts, New York and Ohio. BMJ Open 2022;12(9):e059328.
29. Sprague Martinez L, Rapkin BD, Young A, et al. Community engagement to implement evidence-based practices in the HEALing Communities Study. Drug Alcohol Depend 2020;217:108326.
30. Lefebvre RC, Chandler RK, Helme DW, et al. Health communication campaigns to drive demand for evidence-based practices and reduce stigma in the HEALing Communities Study. Drug Alcohol Depend 2020;217:108338.
31. Winhusen T, Walley A, Fanucchi LC, et al. The Opioid-overdose Reduction Continuum of Care Approach (ORCCA): evidence-based practices in the HEALing Communities Study. Drug Alcohol Depend 2020;217:108325.
32. Wu E, Villani J, Davis A, et al. Community dashboards to support data-informed decision-making in the HEALing Communities Study. Drug Alcohol Depend 2020;217:108331.
33. Moulton LH. Covariate-based constrained randomization of group-randomized trials. Clin Trials 2004;1:297-305.
34. Slavova S, LaRochelle MR, Root ED, et al. Operationalizing and selecting outcome measures for the HEALing Communities Study. Drug Alcohol Depend 2020;217:108328.
35. Westgate PM, Cheng DM, Feaster DJ, Fernández S, Shoben AB, Vandergrift N. Marginal modeling in community randomized trials with rare events: utilization of the negative binomial regression model. Clin Trials 2022;19:162-71.
36. Ford WP, Westgate PM. Improved standard error estimator for maintaining the validity of inference in cluster randomized trials with a small number of clusters. Biom J 2017;59:478-95.
37. Benjamini Y, Hochberg Y. Controlling the false discovery rate: a practical and powerful approach to multiple testing. J R Stat Soc B 1995;57:289-300.

38. Census Bureau. American Community Survey 5-year data 2021. June 15, 2023 (https://www.census.gov/data/developers/data-sets/acs-5year/2021.html).

39. National Center for Health Statistics. U.S. Census populations with bridged race categories (https://www.cdc.gov/nchs/nvss/bridged_race.htm).

40. Census Bureau. 2017–2021 ACS 5-year estimates (https://www.census.gov/programs-surveys/acs/technical-documentation/table-and-geography-changes/2021/5-year.html).

41. Rao IJ, Humphreys K, Brandeau ML. Effectiveness of policies for addressing the US opioid epidemic: a model-based analysis from the Stanford-Lancet Commission on the North American Opioid Crisis. Lancet Reg Health Am 2021;3:100031.

42. Friedman J, Montero F, Bourgois P, et al. Xylazine spreads across the US: a growing component of the increasingly synthetic and polysubstance overdose crisis. Drug Alcohol Depend 2022;233:109380.