

5-29-2020

Regional Variation in States' Naloxone Accessibility Laws in Association With Opioid Overdose Death Rates-Observational Study (STROBE Compliant)

Hyo-Sun You
Chungbuk National University Hospital

Jane Ha
Korea University College of Medicine

Cyra-Y. Kang
University of Nevada, Las Vegas

Leeseul Kim
University of Nevada, Las Vegas
Follow this and additional works at: <https://digitalscholarship.unlv.edu/>

[Jinah Kim](#)
[University of Nevada, Las Vegas](#)
Part of the [Health Policy Commons](#), and the [Public Health Commons](#)

See next page for additional authors
Repository Citation

You, H., Ha, J., Kang, C., Kim, L., Kim, J., Shen, J. J., Park, S., Chun, S., Hwang, J., Yamashita, T., Lee, S. W., Dounis, G., Lee, Y., Han, D., Byun, D., Yoo, J. W., Kang, H. (2020). Regional Variation in States' Naloxone Accessibility Laws in Association With Opioid Overdose Death Rates-Observational Study (STROBE Compliant). *Medicine*, 99(22), 1-6.
<http://dx.doi.org/10.1097/MD.00000000000020033>

This Article is protected by copyright and/or related rights. It has been brought to you by Digital Scholarship@UNLV with permission from the rights-holder(s). You are free to use this Article in any way that is permitted by the copyright and related rights legislation that applies to your use. For other uses you need to obtain permission from the rights-holder(s) directly, unless additional rights are indicated by a Creative Commons license in the record and/or on the work itself.

This Article has been accepted for inclusion in Public Health Faculty Publications by an authorized administrator of Digital Scholarship@UNLV. For more information, please contact digitalscholarship@unlv.edu.

Authors

Hyo-Sun You, Jane Ha, Cyra-Y. Kang, Leeseul Kim, Jinah Kim, Jay J. Shen, Seong-Min Park, Sung-Youn Chun, Jinwook Hwang, Takashi Yamashita, Se Won Lee, Georgia Dounis, Yong-Jae Lee, Dong-Hun Han, David Byun, Ji Won Yoo, and Hee-Taik Kang

Regional variation in states' naloxone accessibility laws in association with opioid overdose death rates—Observational study (STROBE compliant)

Hyo-Sun You, MD^a, Jane Ha, BSc^b, Cyra-Y. Kang, MD^c, Leeseul Kim, MD^c, Jinah Kim, MD^c, Jay J. Shen, PhD^d, Seong-Min Park, PhD^e, Sung-Youn Chun, PhD, MHSA^c, Jinwook Hwang, MD, PhD^f, Takashi Yamashita, PhD, MPH, MA^g, Se Won Lee, MD^h, Georgia Dounis, DDS, MSⁱ, Yong-Jae Lee, MD, PhD^j, Dong-Hun Han, DDS, PhD^{d,k}, David Byun, DO^l, Ji Won Yoo, MD^{n,*} , Hee-Taik Kang, MD, PhD^{a,d,m,*}

Abstract

Though overall death from opioid overdose are increasing in the United States, the death rate in some states and population groups is stabilizing or even decreasing. Several states have enacted a Naloxone Accessibility Laws to increase naloxone availability as an opioid antidote. The extent to which these laws permit layperson distribution and possession varies. The aim of this study is to investigate differences in provisions of Naloxone Accessibility Laws by states mainly in the Northeast and West regions, and the impact of naloxone availability on the rates of drug overdose deaths.

This cross-sectional study was based on the National Vital Statistics System multiple cause-of-death mortality files. The average changes in drug overdose death rates between 2013 and 2017 in relevant states of the Northeast and West regions were compared according to availability of naloxone to laypersons.

Seven states in the Northeast region and 10 states in the Western region allowed layperson distribution of naloxone. Layperson possession of naloxone was allowed in 3 states each in the Northeast and the Western regions. The average drug overdose death rates increased in many states in the both regions regardless of legalization of layperson naloxone distribution. The average death rates of 3 states that legalized layperson possession in the West region decreased (-0.33 per 100,000 person); however, in states in the West region that did not allow layperson possession and states in the Northeast region regardless of layperson possession increased between 2013 and 2017.

The provision to legalize layperson possession of naloxone was associated with decreased average opioid overdose death rates in 3 states of the West region.

Editor: Jongwha Chang.

HTK and JWY as co-corresponding authors equally contributed to this work.

HTK and JWY equally contributed to this research as a corresponding author.

The manuscript has been seen and approved by all authors.

Hee-Taik Kang has received research grants from Ministry of Health and Welfare in Korea.

This research was supported by a grant of the Korea Health Technology R&D project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (grant number: HI19C0526).

The authors have no funding and no conflicts of interest to disclose.

The data that support the findings of this study are available from a third party, but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are available from the authors upon reasonable request and with permission of the third party.

^a Department of Family Medicine, Chungbuk National University Hospital, Cheongju, Chungbuk, ^b Department of Medicine, Korea University College of Medicine, Seoul, Korea, ^c School of Medicine, ^d Department of Health Care Administration and Policy, School of Public Health, ^e Department of Criminal Justice, Greenspun College of Urban Affairs, University of Nevada Las Vegas, Nevada, ^f Department of Thoracic and Cardiovascular Surgery, Korea University College of Medicine, ^g Department of Sociology, Anthropology, and Health Administration and Policy, University of Maryland Baltimore County, Baltimore, Maryland, ^h Department of Physical Medicine and Rehabilitation, Mountain View Hospital, ⁱ School of Dental Medicine, University of Nevada Las Vegas, Las Vegas, Nevada, ^j Department of Family Medicine, Yonsei University College of Medicine, ^k Department of Preventive Dentistry, School of Dentistry, Seoul National University, Seoul, Korea, ^l Department of Medicine, Southern Nevada Veterans Affairs Health System, North Las Vegas, Nevada, ^m Department of Medicine, Chungbuk National University College of Medicine, Cheongju, Chungbuk, Korea, ⁿ Department of Internal Medicine, University of Nevada Las Vegas School of Medicine, 1701 W. Charleston Blvd Ste 230, Las Vegas, NV.

* Correspondence: Hee-Taik Kang, Department of Family Medicine, Chungbuk National University College of Medicine, 1 Chungdae-ro, Seowon-gu, Cheongju, Chungbuk, Rep of Korea (e-mail: kanght0818@gmail.com); Ji Won Yoo, Department of Internal Medicine, University of Nevada Las Vegas School of Medicine, 1701 W. Charleston Blvd Ste 230, Las Vegas, NV 89102 (e-mail: ji.yoo@unlv.edu).

Copyright © 2020 the Author(s). Published by Wolters Kluwer Health, Inc.

This is an open access article distributed under the terms of the Creative Commons Attribution-Non Commercial License 4.0 (CCBY-NC), where it is permissible to download, share, remix, transform, and buildup the work provided it is properly cited. The work cannot be used commercially without permission from the journal.

How to cite this article: You HS, Ha J, Kang CY, Kim L, Kim J, Shen JJ, Park SM, Chun SY, Hwang J, Yamashita T, Lee SW, Dounis G, Lee YJ, Han DH, Byun D, Yoo JW, Kang HT. Regional variation in states' naloxone accessibility laws in association with opioid overdose death rates—Observational study (STROBE compliant). *Medicine* 2020;99:22(e20033).

Received: 4 October 2019 / Received in final form: 1 March 2020 / Accepted: 26 March 2020

<http://dx.doi.org/10.1097/MD.00000000000020033>

Abbreviations: AED = automated external defibrillators, CDC = centers for Disease Control and Prevention, NAL = naloxone accessibility law, OEND = overdose education and nasal naloxone distribution programs.

Keywords: drug policy, naloxone, overdose death, region

1. Introduction

Opioid use disorder and overdose deaths currently pose a grave threat to public health in the US. According to the Centers for Disease Control and Prevention (CDC), approximately 400,000 people died of opioid overdose between 1999 and 2017.^[1] Among the strategies implemented to resolve the issue, an increase in naloxone access by legal means through Naloxone Access Laws (NALs) has been proven to be effective in lowering the incidence of opioid overdose deaths.^[2]

Even with strong measures to address the issue, the number of opioid overdose deaths has been increasing.^[1] However, although the opioid death rates increased in most states, some states were stabilized or even decreased.^[1] According to a CDC report, there was a 71% increase of overdose death rates between 2013 and 2017 and an increase of 9% per year from 1999 to 2011. The CDC indicated, by citing previous studies, that opioid-involved death rate increases were more attributable to illicitly-manufactured fentanyl than to pharmaceutically-manufactured fentanyl.^[3–5] Fentanyl is 50 to 100 times more potent than morphine and has a rapid onset of action, leading to immediate respiratory depression and death. Thus, Reduction of opioid-related mortality rates requires cooperation among public health and legislative officials, in addition to improving naloxone accessibility. Public health authorities should develop more efficient surveillance systems for detecting and controlling drug overdose outbreaks, and legislative officials need to enact laws designed to reduce and control these outbreaks. One of the best options to halt explosive growth of opioid-involved overdose deaths is to allow laypersons to possess naloxone without prescription.

States with the highest observed age-adjusted drug overdose death rates require stronger measures to combat the burgeoning opioid epidemic. In particular, some states in the Northeast, such as Pennsylvania, New Hampshire, Maine, Massachusetts and Connecticut, fall into this category.^[6] However, previous studies have found regional imbalances between opioid overdose treatment capacity and need, especially in the Northeast states of Pennsylvania, New York and New Jersey.^[7] Naloxone, a competitive opioid antagonist, can rapidly reverse opioid overdose toxicity.^[8] The implementation of NALs increased accessibility of naloxone to the public in the US Naloxone administration by bystanders improved the recovery rate from opioid overdose.^[9] However, state naloxone dispensing rates do not match opioid overdose death rates.^[10] While overdose education and naloxone distribution programs raised awareness and accessibility, there is possibility of a mismatch between naloxone possession and use by laypersons.^[11] The scope and extent of immunity provided by state legislations also differ; some allow laypersons to possess naloxone without prescription, but others allow only distribution.^[12] On April 5, 2018, the Office of the Surgeon General released a statement to urge further expansion of naloxone availability.^[13] The first step in furthering this expansion should be to amend law to permit layperson naloxone

possession, especially in regions where opioid overdose death reduction is most needed.

The objective of our study was to evaluate these regional differences and recent trends in drug overdose death rates in states with or without NALs.

2. Methods

2.1. Data source

Study design was a serial retrospective cross-sectional data analysis.^[14] We obtained data from the National Vital Statistics Systems presenting provisional counts for drug overdose deaths occurring in 50 states and the District of Columbia from 2013 to 2017. The counts represented the number of reported deaths due to drug overdose occurring in the 12-month periods ending in the months indicated. Information on state NALs was obtained from the Prescription Drug Abuse Policy Surveillance Systems as well as academic and legal sources. Additionally, we referred to the US Census Bureau Region and Census Division for regional classifications in reference to states with and without NALs. Approval by an Institutional Review Board was not necessary because all data were secondary, de-identified, and publicly available and patients' consent was not involved.

2.2. Main measurement and variables of interest

Drug overdose deaths were identified in the National Vital Statistics System multiple cause-of-death mortality files from data contained on death certificates.^[14] The National Vital Statistics System is an inter-governmental system to share data regarding the vital statistics of the US population.^[14] The cause of death is coded based on the International Classification of Disease-10 codes X40-44 (unintentional), X60-64 (suicide), X85 (homicide), or Y10-14 (undetermined intent). Among deaths with drug overdose as the underlying cause, the type of drug or drug category is demonstrated by the following International Classification of Disease, 10th revision, Clinical Modification multiple cause-of-death codes: T40.0, narcotics and psychodysleptics; T40.1, heroin; T40.2, other opioids such as natural and semisynthetic opioids; T40.3, methadone; T40.4, other synthetic narcotics, excluding methadone; T40.5, cocaine; and T43.6, psychostimulants with abuse potential. Some causes of deaths involved more than 1 type of drug, and these were included in rates for each drug category; thus, causes of death in some cases were not mutually exclusive. For example, a death involving both a synthetic opioid other than methadone and heroin would be included in both the synthetic opioid other than methadone and heroin death rates. All annual drug overdose death rates were presented as number of deaths per 100,000 persons. We examined the outcomes of interest, state-level annual drug overdose death by region, as defined by the Healthcare Cost and Utilization Project sponsored by the Agency for Healthcare Research and Quality. We focused on the Western and Northeastern states, which are unlikely to have neighboring effects on each other, to discern which regions need stronger legislative measures.

Table 1
Age-adjusted drug overdose death rates according to state by layperson distribution.

Northeast (n = 9)				No layperson distribution			
Layperson distribution				No layperson distribution			
State	Average change		13.57	State	Average change		15.15
	2013	2017	Difference		2013	2017	Difference
Maine	9.9	29.9	20	Connecticut	12.3	27.7	15.4
New Hampshire	11.8	34	22.2	Massachusetts	13.3	28.2	14.9
New Jersey	7.6	22	14.4				
New York	8.3	16.1	7.8				
Pennsylvania	7.8	21.2	13.4				
Rhode Island	18.1	26.9	8.8				
Vermont	11.6	20	8.4				

West (n = 13)				No layperson distribution			
Layperson distribution				No layperson distribution			
State	Average change		0.34	State	Average change		6.17
	2013	2017	Difference		2013	2017	Difference
Alaska	9.2	13.9	4.7	Arizona	8.2	13.5	5.3
California	4.9	5.3	0.4	Idaho	5.7	18.8	13.1
Colorado	8	10	2	Wyoming	8.6	8.7	0.1
Hawaii	4.7	3.4	-1.3				
Montana	7.2	3.6	-3.6				
New Mexico	16	16.7	0.7				
Nevada	13.7	13.3	-0.4				
Oregon	7.5	8.1	0.6				
Utah	15.9	15.5	-0.4				
Washington	8.9	9.6	0.7				

* State abbreviations are in alphabetical order.
 * All death rates are per 100,000 populations.

2.3. Statistical analysis

We adopted the statistical results from a previous study.^[1] The study performed statistical analysis of state-level average annual percentage changes in age-adjusted drug overdose death rates from 2013 to 2017.^[1] Annual percentage changes with statistically significant trends were analyzed using z-tests when the number of deaths was ≥100 and non-overlapping confidence intervals based on a gamma distribution when the number was <100. Scholl L et al described the statistical analysis in more detail.^[1]

3. Results

Seven states in the Northeast region and 10 states in the Western region allowed layperson distribution of naloxone. Layperson possession of naloxone was allowed in 3 states each in the Northeast and the Western regions.

Table 1 presents age-adjusted drug overdose death rates according to state by layperson distribution availability. In the Northeast region, seven states that allowed layperson distribution of naloxone showed an increase in age-adjusted drug overdose death rate between 2013 and 2017. The average increase in the death rate was 13.57 per 100,000 persons. Two states in the Northeast region that did not allow layperson distribution of naloxone showed an average increase in death rate of 15.12 per 100,000 persons, which was slightly higher than that of the states with naloxone distribution. The Western states generally showed smaller changes in age-adjusted drug overdose death rates than those of the Northeast. The 3 Western states that allowed naloxone distribution showed an average increase in

death rate of 0.34 per 100,000 persons; this was significantly lower than that of the Western states that did not allow naloxone distribution (6.17 per 100,000 persons).

Table 2 shows age-adjusted drug overdose death rates according to state by layperson possession. Three Western states that allowed possession of naloxone showed a -0.33 per 100,000 persons decrease in average overdose death rate. This is the only group that showed a decrease in drug overdose death rate from 2013 to 2017. The other 10 Western states that did not allow naloxone possession showed an increase in death rates at an average of 2.53 per 100,000 persons. In the Northeastern region, 3 states that allowed layperson possession of naloxone showed significantly smaller increases in death rates, an average of 10.7 per 100,000 persons, compared to the 15.53 per 100,000 persons average of 6 states that did not allow naloxone possession.

4. Discussion

We found regional variation of drug overdose death rates that appeared to be associated with scope and extent of NAL provisions. In the Western region, drug overdose death rates decreased in the states that allowed layperson naloxone possession. Sharp increases in drug overdose death rates in the Northeastern region were partially alleviated in the states allowing layperson naloxone possession.

Despite efforts to solve the opioid epidemic issue, numbers of hospitalizations and emergency department visits and net opioid overdose death rates are on the rise.^[4,15,16] However, the pace at which the overdose death rates has grown differs by

Table 2
Age-adjusted drug overdose death rates according to state by layperson possession.

Northeast (n=9)				West (n=13)			
Layperson possession				No layperson possession			
State	Average change		10.7 Difference	State	Average change		15.53 Difference
	2013	2017			2013	2017	
Massachusetts	13.3	28.2	14.9	Connecticut	12.3	27.7	15.4
Rhode Island	18.1	26.9	8.8	Maine	9.9	29.9	20
Vermont	11.6	20	8.4	New Hampshire	11.8	34	22.2
				New Jersey	7.6	22	14.4
				New York	8.3	16.1	7.8
				Pennsylvania	7.8	21.2	13.4

Layperson possession				No layperson possession			
State	Average change		-0.33 Difference	State	Average change		2.53 Difference
	2013	2017			2013	2017	
Hawaii	4.7	3.4	-1.3	Alaska	9.2	13.9	4.7
New Mexico	16	16.7	0.7	Arizona	8.2	13.5	5.3
Nevada	13.7	13.3	-0.4	California	4.9	5.3	0.4
				Colorado	8	10	2
				Idaho	5.7	18.8	13.1
				Montana	7.2	3.6	-3.6
				Oregon	7.5	8.1	0.6
				Utah	15.9	15.5	-0.4
				Washington	8.9	9.6	0.7
				Wyoming	8.6	8.7	0.1

*State abbreviations are in alphabetical order.
 *All death rates are per 100,000 populations.

states. This difference in pace can partially be explained by the differences in extent to which lay people have access to naloxone. States that allowed layperson possession without prescription demonstrated slower increases in opioid overdose death rates compared to those that did not.^[17] Increasing possession of naloxone by lay responders is more directly related to reducing overdose death than increasing distribution. Although awareness and accessibility of naloxone rose, naloxone possession may be different from its actual use.^[11] Some speculate that individuals may be reluctant to carry naloxone in fear of harassment from law enforcement due to the association between naloxone and opioid use. Therefore, reducing the stigma attached to possession by legal means will be pivotal to overdose prevention. Efforts should be made to make naloxone more available not only by means of treatment and prescription but also by involving laypersons.

Previous findings suggested that witnessing an overdose or knowing someone affected by overdose were potential motivators for first-time naloxone access among lay responders.^[18] However, the general public, including opioid users, may not be aware of naloxone access. Programs like overdose education and nasal naloxone distribution programs (OEND) have attempted to educate opioid users and bystanders to prevent, recognize, and respond to overdose with use of naloxone. According to the interrupted time series analysis performed by Walley et al., communities where OEND was implemented displayed reduced opioid overdose death rates compared to those with no OEND.^[19] There needs to be a nationwide effort led by policy-makers to expand naloxone education programs like OEND targeting not only opioid users and their families but also general public.^[20]

Naloxone has become more available with implementation of NALs. However, naloxone's distribution system needs to be optimized. Automated external defibrillators (AEDs) have become widely available and encouraged for public use. Thus, naloxone kits can be added to the AED cabinets.^[21] However, locating AEDs in public place can be difficult in certain locations, resulting in greater delay before implementation.^[22] If AEDs were used as landmarks for naloxone kits, the same issue will be present for administration in an emergent overdose scenario. To counteract this, a national registry of naloxone kit locations should be implemented as well. Smartphone technology with a global positioning system directing bystanders to the location of the emergency, which has been shown to increase the rates of cardiopulmonary resuscitation by bystanders, could also be used to help bystanders locate the nearest naloxone kit.^[23] Applications, such as NaloxoFind, have been used to identify and locate naloxone within a 2 mile radius and allows communication with those carrying naloxone.^[24] Further promotion of such technology will increase use of available naloxone in public.

These results indicate that legislation needs to be revised to maximize naloxone availability by permitting laypersons to possess naloxone without prescription, especially in states where the problems are rising. With statewide adoption of legislation designed to improve layperson naloxone access, policy-makers need to assess the effectiveness in delivery and impact of these policies. The opioid epidemic is a nationwide catastrophe. It can affect our lives directly or indirectly. To alleviate the opioid crisis, multidisciplinary approaches by personnel from a variety of fields such as government, community, and academia are required. Health professionals, especially opioid prescribers, are also at the forefront of the fight against the opioid epidemic. These

professionals should be well-versed in naloxone prescription practices and education on its proper use. In addition to legislation of NALs, fund-raising, community education and training for stakeholders, providing treatment programs and facilities, and policy-making are necessary. A community coalition model such as Project Nazzarus provides a good example for us to improve opioid overdose outcomes.^[2,5] Project Nazzarus involves community activation and coalition building, monitoring and surveillance system, overdose prevention, rescue medication for reversing drug overdoses, and assessment of project components. In Project Nazzarus, stakeholders from various sectors such as healthcare, school, police, and substance abuse facilities, have participated in this model and committed to engage the support from relevant parts in the community. Through a community forum, they share information, raise awareness of the community's problems, and bring the attention of other people. In addition, they establish a working coalition and a community plan and make policies to resolve problems. Providing naloxone to the public and teaching them its proper use will improve responsibility and power to reduce the opioid epidemic. In order to develop sustainable policies, cost-effectiveness should be considered. Increased naloxone distribution and possession may increase medical expenditures and the public health budget. Because opioid use is high contagious and the consequences can be fatal, health authorities need to pay the cost even if NALs are not cost-effective. In addition, the ethical and psychological aspects should be considered. The social effort to reduce the stigma regarding opioid use and naloxone possession and emotional supports for drug users to return to their communities are required. Understanding the biopsychosocial nature of substance disorder and evidence-based interventions to resolve this growing problem are necessary.

We acknowledge several limitations. First, we did not use primary death certificate data but used the secondary data. This limitation can result in some biases. Second, low sensitivity and high specificity in weighted estimates occurred when identifying persons who use illicit drugs from administrative claim data.^[26] Third, other factors involved in reducing opioid overdose death rates have not been considered and, therefore, not controlled. This is particularly true in terms of assessing the actual impact of legalization of layperson naloxone possession on death rates. Beyond NALs, other conditions may have influenced clinical outcomes. In addition, only northeast and west regions were investigated in this study in order to minimize neighboring effects. Thus, further studies should be warranted to assess that increased naloxone accessibility decreases opioid overdose deaths in other regions after controlling for confounding factors. Fourth, whether or not more laypersons possessed and used naloxone for rescue after establishment of NALs is difficult to surmise, although there is some indirect evidence. Nationwide naloxone dispensing increased nearly 8-fold from the 4th quarter of 2015 to the 2nd quarter of 2017.^[10] The Surgeon General emphasized the importance of awareness and distribution of naloxone to the public. This study demonstrated that layperson possession might be associated with reduced growth of the opioid overdose death rate. In addition, because of the possibility of under-reporting of overdose deaths or lag times from coroner reports, the data may underestimate opioid overdose deaths. Fifth, we used the state-level data that could distort the results than the county- or city-level data. Despite these potential limitations, the strength of this study is provision of several new insights into the opioid crisis from a public health perspective. This study demonstrated the

association between NAL provisions (possession vs distribution) and their effects on opioid overdose death according to geographic location (Northeast vs West).

In conclusion, we found that the greater was the access to naloxone, the lower were the drug overdose death rates. Age-adjusted drug overdose death rates in states that allowed layperson distribution were lower than those in states that did not. These death rates showed a similar pattern according to layperson possession; the death rates were lower in states that allowed layperson possession than in states that did not. These findings support the assertion that improved naloxone accessibility will ameliorate drug overdose death.

Acknowledgment

This research was supported by a grant of the Korea Health Technology R&D project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (grant number: HI19C0526)

Author contributions

Conceptualization: Cyra-Yoonsun Kang, Leeseul Kim, Jinah Kim, Jinwook Hwang, Georgia Dounis, Yong-Jae Lee, Hee-Taik Kang.

Data curation: Cyra-Yoonsun Kang.

Formal analysis: Hyo-Sun You, Cyra-Yoonsun Kang, Dong-Hun Han, Ji Won Yoo.

Methodology: Hyo-Sun You, Cyra-Yoonsun Kang, Takashi Yamashita, Dong-Hun Han.

Project administration: Ji Won Yoo.

Resources: Cyra-Yoonsun Kang, Jay J. Shen, Seong-Min Park, Se Won Lee, David Byun.

Software: Sung-Youn Chun.

Supervision: Cyra-Yoonsun Kang, Georgia Dounis, Ji Won Yoo.

Validation: Leeseul Kim, Jinah Kim, Jay J. Shen, Seong-Min Park, Jinwook Hwang, Takashi Yamashita, Se Won Lee, David Byun.

Visualization: Cyra-Yoonsun Kang, Leeseul Kim, Jinah Kim, Sung-Youn Chun.

Writing – original draft: Cyra-Yoonsun Kang, Jay J. Shen, Seong-Min Park, Sung-Youn Chun, Jinwook Hwang, Takashi Yamashita, Ji Won Yoo.

Writing – review and editing: Hyo-Sun You, Cyra-Yoonsun Kang, Leeseul Kim, Jinah Kim, Yong-Jae Lee, Dong-Hun Han, David Byun, Hee-Taik Kang.

References

- Scholl L, Seth P, Kariisa M, et al. Drug and opioid-involved overdose deaths - United States, 2013-2017. *MMWR Morb Mortal Wkly Rep* 2018;67:1419–27.
- McClellan C, Lambdin BH, Ali MM, et al. Opioid-overdose laws association with opioid use and overdose mortality. *Addict Behav* 2018;86:90–5.
- Gladden RM, Martinez P, Seth P. Fentanyl law enforcement submissions and increases in synthetic opioid-involved overdose deaths - 27 states, 2013-2014. *MMWR Morb Mortal Wkly Rep* 2016;65:837–43.
- 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.

- [5] Peterson AB, Gladden RM, Delcher C, et al. Increases in fentanyl-related overdose deaths - Florida and Ohio, 2013-2015. *MMWR Morb Mortal Wkly Rep* 2016;65:844-9.
- [6] Opioid Overdose Death Rates and All Drug Overdose Death Rates per 100,000 Population (Age-Adjusted) The Henry J. Kaiser Family Foundation. 2019. Available at: <https://www.kff.org/state-category/health-status/opioids>. Accessed October 1, 2019
- [7] Langabeer JR, Gourishankar A, Chambers KA, et al. Disparities between US opioid overdose deaths and treatment capacity: a geospatial and descriptive analysis. *J Addict Med* 2019;13:476-82.
- [8] Kim HK, Nelson LS. Reducing the harm of opioid overdose with the safe use of naloxone: a pharmacologic review. *Expert Opin Drug Saf* 2015;14:1137-46.
- [9] Giglio RE, Li G, DiMaggio CJ. Effectiveness of bystander naloxone administration and overdose education programs: a meta-analysis. *Inj Epidemiol* 2015;2:10.
- [10] Freeman PR, Hankosky ER, Lofwall MR, et al. The changing landscape of naloxone availability in the United States, 2011-2017. *Drug Alcohol Depend* 2018;191:361-4.
- [11] Tobin K, Clyde C, Davey-Rothwell M, et al. Awareness and access to naloxone necessary but not sufficient: examining gaps in the naloxone cascade. *Int J Drug Policy* 2018;59:94-7.
- [12] Legal Interventions to reduce overdose mortality: Naloxone access and overdose good Samaritan laws. The network for public health law. August 25, 2017. Available at: https://www.networkforphl.org/_asset/qz5pvn/legal-interventions-to-reduce-overdose.pdf Accessed October 1, 2019.
- [13] Rubin R. Surgeon general urges expanded availability of naloxone. *JAMA* 2018;319:2068.
- [14] National Vital Statistics System. Available at: https://www.cdc.gov/nchs/nvss/mortality_public_use_data.htm. Accessed Jan 31, 2020.
- [15] Mazer-Amirshahi M, Sun C, Mullins P, et al. Trends in emergency department resource utilization for poisoning-related visits, 2003-2011. *J Med Toxicol* 2016;12:248-54.
- [16] Vivolo-Kantor AM, Seth P, Gladden RM, et al. Vital signs: trends in emergency department visits for suspected opioid overdoses—United States, July 2016–September 2017. *MMWR Morb Mortal Wkly Rep* 2018;67:279-85.
- [17] Abouk R, Pacula RL, Powell D. Association between state laws facilitating pharmacy distribution of naloxone and risk of fatal overdose. *JAMA Intern Med* 2019;179:805-11.
- [18] Watson DP, Ray B, Robison L, et al. Lay responder naloxone access and good Samaritan law compliance: postcard survey results from 20 Indiana counties. *Harm Reduct J* 2018;15:18.
- [19] Walley AY, Xuan Z, Hackman HH, et al. Opioid overdose rates and implementation of overdose education and nasal naloxone distribution in Massachusetts: interrupted time series analysis. *BMJ* 2013;346:f174.
- [20] Bagley SM, Peterson J, Cheng DM, et al. Overdose education and naloxone rescue kits for family members of individuals who use opioids: characteristics, Motivations, and Naloxone Use *Subst Abus* 2015;36:149-54.
- [21] VA Adding opioid antidote to defibrillator cabinets for quicker overdose response. Sep 27, 2018. Available at: <https://www.npr.org/sections/healthshots/2018/09/27/650639122/va-adding-opioid-antidote-to-defibrillator-cabinets-for-quicker-overdose-respons> Accessed October 1, 2019.
- [22] Leung AC, Asch DA, Lozada KN, et al. Where are lifesaving automated external defibrillators located and how hard is it to find them in a large urban city? *Resuscitation* 2013;84:910-4.
- [23] Ringh M, Rosenqvist M, Hollenberg J, et al. Mobile-phone dispatch of laypersons for CPR in out-of-hospital cardiac arrest. *N Engl J Med* 2015;372:2316-25.
- [24] Find Naloxone When You Need It with Naloxofind. Available at: <https://www.altrixmedical.com/naloxofind> Accessed October 1, 2019.
- [25] Albert S, Brason FW 2nd, Sanford CK, Dasgupta N, Graham J, Lovette B. Project Nazarus: community-based overdose prevention in rural North Carolina. *Pain Med* 2011;12(Suppl 2):S777-85.
- [26] Kim HM, Smith EG, Stano CM, et al. Validation of key behaviourally based mental health diagnoses in administrative data: suicide attempt, alcohol abuse, illicit drug abuse and tobacco use. *BMC Health Serv Res* 2012;12:18.