**Study Goals**

The National Drug Early Warning System (NDEWS) Naloxone Phase II Replication Studies were designed to explore the feasibility of rapidly addressing research questions by adding questions to ongoing studies already in the field. Information about the awareness and availability of naloxone, attitudes towards naloxone, and naloxone's influence on drug use was collected from a local (Baltimore, MD) and a national (Researched Abuse, Diversion and Addiction-Related Surveillance [RADARS®] System) sample of persons seeking treatment for opioid use disorder (OUD). A smaller, Phase I study formed the basis for the Phase II replication studies.

**Findings**

- 71% or more of participants in both sites were aware of naloxone and knew how to get it; far lower percentages reported actually carrying naloxone with them (53% locally, 22% nationally).
- More than half of the Baltimore respondents reported that naloxone availability changed how they think about overdose; approximately half of the national respondents who had heard of naloxone reported engaging in harm reduction pacing behaviors.
- Many Baltimore participants reported concerns about administering naloxone, including naloxone-precipitated withdrawal and other potential medical consequences. Others expressed feelings of increased comfort or safety in their drug use by having naloxone on hand but believe it could facilitate riskier behavior in others.
- Many participants described naloxone as a tool or “safety net.”

**Implications for Public Health**

The findings further support the initial Phase I findings underscoring the need to expand educational outreach and intervention about current laws and the effective use of naloxone to respond to overdoses. Policies may also need to be updated to improve access to naloxone and to reduce stigma and legal concerns of those possessing and administering naloxone.

**Implications for Future Research**

It was feasible to collect information on important research topics by introducing a standard module of questions to ongoing studies already in the field. Future studies might embrace this methodology.

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**Overview**

The NDEWS Naloxone Phase I Pilot study was launched in 2018 in response to interest from policymakers to learn about the availability and impact of naloxone on opioid users. The NDEWS Coordinating Center worked closely with a team of researchers to develop a set of questions that could be administered quickly by three studies already in the field: 1) an NDEWS HotSpot study of syringe exchange clients, 2) a National Institute of Drug Abuse (NIDA)-funded study of emergency department (ED) patients, and 3) a study of patients at a Baltimore opioid treatment program.

The goal was to rapidly collect information from current and recent opioid users about the awareness and availability of naloxone, attitudes towards naloxone, and its influence on drug use patterns. Each ongoing study successfully implemented the questions and collected valuable information. However, the samples were small and questions remained about the feasibility of this approach with larger, even national studies. In late 2019, the Phase II replication study was launched with a larger local sample in Baltimore, MD and a national sample to be reached through a new collaboration with RADARS System.

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**Naloxone Themes**

1. Background information
2. Knowledge about naloxone
3. Access to naloxone (First-person)
4. Access to naloxone (Third-person)
5. Experience with naloxone
6. Perceptions and Attitudes Toward naloxone (First-person)
7. Perceptions and Attitudes Toward naloxone (Third-person)
8. Influence of the Availability of naloxone on Drug Use Behaviors
9. Adverse Consequences of Alcohol and/or Drug Abuse
10. Cascade of Care (from naloxone awareness to naloxone carry)
Four steps were completed as a part of this study: 1) Phase I findings and recommendations were reviewed by a NDEWS Naloxone Workgroup, 2) Revisions were made to the questions by the two site teams, 3) Study protocols were developed, and 4) Findings were analyzed and reported. The COVID-19 pandemic hit shortly after data collection began, leading to a shutdown of all research and requiring the researchers to revise their protocols to be line with local safety protocols.

**Methods**

The replication study was conducted with larger samples in two sites.

**Local sample: Baltimore, MD.** This study, conducted by researchers at the University of Maryland, Baltimore, led by Dr. Annabelle Belcher, used a convenience sampling method with a detailed mixed methods (quantitative and qualitative) structured interview questionnaire administered to local residents seeking OUD-treatment. Participation was voluntary and anonymous, and participants were paid five dollars for their time. The 97 participants were adults older than 18 years of age who were enrolled in medication-based treatment at the University of Maryland Drug Treatment Center (UMDTC). “Prior to the COVID-19 pandemic, participants met with a research team member for one meeting, and survey administration took approximately 20 to 25 minutes. During the pandemic, participants were interviewed virtually via telephone” (Belcher et al, 2021). Most participants (67) were recruited in-person in three weeks pre-pandemic, and 33 were recruited by telephone in three weeks during the pandemic. No differences in age of participants or other demographics were found between in-person and virtual (telephone) encounters. Inclusion criteria were the same for both groups. Therefore, all data are aggregated. The demographics of the respondents are provided in Table 1. Additional details about participant recruitment and necessary changes during the pandemic are provided in the full study report. (Belcher et al., 2021)

**National sample: RADARS®.** The national study conducted by researchers at Researched Abuse, Diversion, and Addiction-Related Surveillance (RADARS®) System led by Dr. Janetta Iwanicki utilized a voluntary and anonymous self-administered questionnaire completed within the first week of admission by individuals seeking OUD treatment across the U.S. The scope of the RADARS System is shown in Figure 1. The naloxone questions were added to the standard RADARS System Treatment Center Programs Combined (Opioid Treatment Program and Survey of Key Informants’ Patients Program) data collection quarterly questionnaires April-September 2020. The Opioid Treatment Program respondents were entering medication-assisted treatment for OUD. The Key Informants’ respondents reported an opioid as their primary drug of abuse and came from a diverse network of public and private treatment programs. A total of 2,278 questionnaires were completed during the study period. Standard exclusion criteria included missing or invalid residential zip codes, missing age, and age under 18. Patients who did not report past month drug abuse and questionnaires suggestive of careless or extreme response patterns were also excluded. The remaining 1,310 questionnaires included 967 from the Opioid Treatment Program and 343 from the Survey of Key Informants’ Patients Program. The demographics of the respondents are provided in Table 1. Additional information about participant recruitment and the impact of the COVID-19 pandemic are provided in the full study report. (Severtson et al., 2021)
Results

Baltimore, MD: The majority of Baltimore participants were male (59%) and African American (62%) with a mean age of 47.6. Three quarters were lifelong residents of Baltimore and more than half (53%) reported ever overdosing on opioids. More than three quarters were not working. Key findings discussed in the study report include:

- Naloxone Awareness to Naloxone Carry (Cascade of Care): All of the 97 respondents reported having heard of naloxone, and 88% reported knowing where to get it. Slightly lower percentages reported receiving training on naloxone administration (83.5%) and currently owning naloxone (79%). Only half (53%) reported actually carrying naloxone. These declines were also found in the Phase I Baltimore study: “…although all survey participants were familiar with naloxone and its purpose, the data revealed a steep decline in the intermediate steps (Availability, Obtainability, Training, Possession) to consistent carrying of naloxone” (Belcher et al., 2021).

- Perceptions and Attitudes: More than half (56%) of the respondents reported that naloxone availability changed how they think about overdose, but less than one-third (29%) believed that it changed how others think about overdose. In general, participants characterized more positive changes in their own thinking than in the thinking of others in terms of feeling safer when naloxone is available (50% vs. 35%) and being more aware of the high risks of opioid use (21% vs. 19%). In contrast, participants’ responses about engaging in harm reduction practices were very similar for themselves and others in terms of the use of fentanyl strips and watching someone else use first. However, participants were more likely to report others taking a test amount, going slow, or only using opioids when others are around than to say that they do so themselves.

- Barriers to Naloxone: Although more than three-quarters of the participants reported receiving naloxone training, many reported the need for more education on how to obtain and administer naloxone was needed to encourage the use of naloxone. For example, participants had differing opinions on the impact of naloxone on opioid use and some suggested that more information was needed on how to deal with people after giving them naloxone (see sidebar on next page).

- Naloxone Experiences: Respondents reported being hesitant to administer naloxone due to concerns about determining if the individual is really experiencing an overdose, putting the individual into withdrawal, and the reactions and medical consequences they may have. They also shared theories about the effectiveness of injectable versus spray naloxone (see sidebar). However, many respondents validated the importance of
naloxone referring to it as a “wonder drug” or band-aid” and reporting that it is “a great help in the community” and everyone should carry it.

**RADARS® System.** The majority of the RADARS System participants were male (56%), white (75%), were aged 26-49 (75%), and were from the southern or western U.S. (71%). More than one-third reported a history of opioid overdose. Key findings discussed in the study report include:

- **Naloxone Awareness to Naloxone Carry (Cascade of Care):** Approximately three-quarters of respondents reported having heard about naloxone (76.4%) and knowing at least one place to obtain it (71.1%), but far lower percentages reported receiving naloxone training (35.5%), currently owning it (36.6%), and carrying it with them (22%). Higher percentages in the Northeast reported each of these items than other regions of the U.S. History of overdose and use of illicit opioids as primary drug were also associated with greater awareness of naloxone.

- **Harm Reduction:** Among the 1,001 respondents who reported having heard of naloxone, approximately half endorsed harm reduction pacing behaviors such as taking smaller amounts, taking test amounts, and taking slower. Using around others (20%) and using fentanyl strips (5%) were less likely to be endorsed.

- **Barriers to Naloxone:** More than two-thirds of respondents who had heard of naloxone reported knowing how to administer it (71%) and when to give it (68%). Respondents were much less likely to report that others knew these things and more likely to report that others experienced emotional and mental barriers to obtaining naloxone.

- **Naloxone Experiences:** Approximately two-thirds of respondents aware of naloxone reported having naloxone available and feeling safer with naloxone nearby when using opioids. Most reported that naloxone was easy to get (71%) and that they could get it for free (78%), but a slightly smaller percentage actually knew someone who carried it (61%). Less than half reported having seen naloxone administered (48%), having been in a situation where naloxone was needed but not available (46%), or having given naloxone themselves (36%).

**Conclusions and Implications for Future Research**

Both the national and local studies demonstrated that it is feasible to collect information on important research topics by introducing a standard module to ongoing studies already in the field. The results of the Phase I studies were reviewed and discussed by the research teams in both Phase II studies and mutually agreed upon revisions were made to the naloxone questionnaire. Although delays of several months were experienced due to the pandemic, data collection and analyses were completed in approximately 12 months.

Respondents in both samples were predominantly male, and similar percentages had completed a GED/high school and lived in their own domicile. However, the Baltimore sample was slightly older, majority African American, and a higher percentage reported a history of opioid overdose than the RADARS System sample.
The results of both the local Baltimore study and the national RADARS System study are similar to those of the original Phase I studies. The highest percentages of respondents reported having heard of naloxone and knowing at least one place to get it while very few reported actually carrying naloxone with them. Interestingly, the respondents in the RADARS System national study showed a greater tendency towards othering than the Baltimore study. While higher percentages of respondents in the national sample endorsed pacing behaviors by themselves, the percentages reported by the local respondents for themselves and other were much more similar.

“Although most study participants had a favorable view regarding the availability, use and importance of naloxone as a life-saving medication, many participants also revealed internalized stigma regarding the use of naloxone, with several people endorsing the idea that naloxone is used as a safety net that allows for riskier substance use behaviors” (Belcher et. al., 2021). Future research should continue to investigate the role of stigma and the personal experience of stigma in an individual’s perceptions and willingness to administer naloxone to prevent or reverse overdoses.

**Implications for Public Health**

Although a small number of participants were included in this study, the results of the three pilot sites were consistent in suggesting a possible need to expand educational outreach about current laws and the effective use of naloxone to respond to overdoses. The researchers recommend that education focus on improving awareness and understanding of local laws such as Good Samaritan Laws, increasing access to naloxone, improving the understanding of using naloxone to reverse overdoses, and reinforcing the use of measures users can take to protect themselves from overdosing.

Policies may also be needed to improve access to naloxone through community settings and peer distribution programs to reach diverse populations, including those who may be reluctant to access clinics and pharmacies. Programs might also consider addressing stigma felt by those experiencing overdoses and acquiring and administering naloxone and build an awareness that carrying naloxone signals recovery and a willingness to save others’ lives.

Reinforcing the use of safety measures by people who use opioids could go beyond the proper use of naloxone to also include education about both safer drug use practices (e.g., test injections, having naloxone readily available) and fentanyl-specific techniques (e.g., strips and information about local drug potency and mixtures).

### Full Study Reports

Belcher, Annabelle, Ph.D.; Thomas O. Cole, MA; Mark Yoon, MA; Alexander Pappas, MD; Zofia Kozak, MD; Christopher Welsh, MD, Eleanor Erin Artigiani, MA, and Eric D. Wish, Ph.D. Characterizing Knowledge, Attitudes, Behaviors, and Practices Related to Bystander Naloxone in Methadone-Maintained Individuals with Opioid Use Disorder. University of Maryland, Baltimore: February 2021.


### Study Site Teams

**Baltimore, Maryland: Annabelle Belcher, PhD**, Assistant Professor of Psychiatry at the University of Maryland School of Medicine, PI; based at the University of Maryland Drug Treatment Center in west Baltimore along with Thomas O. Cole, MA, Mark Yoon, MPH, Alexander Pappas, MD, Zofia Kozak, MD and Christopher Welsh, MD.

**RADARS®: Jeanetta Iwanicki, MD**, Emergency Medicine Physician at Denver Health, PI, with Stevan Geoffrey Severtson, Marie Gurrola, David Grundy, and Heather Olsen.

**The Center for Substance Abuse Research (CESAR)** is one of the nation’s premier university-based substance use and misuse research institutes that addresses substance use and misuse, with a focus on emerging trends. CESAR, the NDEWS Coordinating Center 2014-2020, works with a network of experts to develop and conduct studies such as the naloxone pilot study. Additional information about CESAR and all CESAR publications are available at [www.cesar.umd.edu](http://www.cesar.umd.edu). To stay informed about emerging trends, join the CESAResearch Network or follow us @CESAResearch.

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**All Naloxone Phase I Pilot Studies and Phase II reports are available online:**
[www.cesar.umd.edu](http://www.cesar.umd.edu)

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