Empowering Community Pharmacists to Prevent Opioid Overdose Deaths: A Mixed Methods Study Exploring Implementation of Community Pharmacy-Based Naloxone Services

by

Lindsey Hohmann, PharmD, MTMC

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Approved by

Salisa Westrick, Chair, Professor of Health Outcomes Research & Policy
Kimberly B. Garza, Associate Professor of Health Outcomes Research & Policy
Brent Fox, Associate Professor of Health Outcomes Research & Policy
Chih-hsuan Wang, Associate Professor of Educational Research, Measurement, and Assessment
Geoffrey Curran, Professor of Pharmacy Practice & Psychiatry, University of Arkansas

Abstract

Background and Significance: Given the rising problem of prescription drug abuse and high number of opioid-related deaths annually in the United States, mechanisms to distribute naloxone are sorely needed. Community pharmacists represent one avenue to increase patient access to naloxone. However, many pharmacists miss opportunities to dispense naloxone.

Objective and Specific Aims: The **purpose** of this study is to create and assess the effectiveness of a targeted pharmacist training program for naloxone therapy management to increase community pharmacists' knowledge, intention, attitudes, confidence, and naloxone dispensing activities for prevention of opioid overdose deaths. This study was conducted using mixed methods and a two-group pragmatic randomized controlled trial design among community pharmacists in Alabama to address **two specific aims**: **1)** to incorporate community pharmacists' training needs and experts' strategies to overcome barriers regarding community pharmacy-based naloxone services implementation into the development of a targeted training program; and **2)** to evaluate a targeted naloxone training program among community pharmacists.

Methods: Participants included community pharmacists in Alabama counties with high opioid overdose death rates. Pharmacists' naloxone training needs (format and content), attitudes, barriers/facilitators, and current naloxone service implementation strategies were explored using semi-structured telephone interviews with community pharmacists. Opioid/naloxone experts were also interviewed to compare current practices to recommended implementation strategies. Results from qualitative analysis informed development of a training program, using a **participatory design approach** with a panel of pharmacists and experts to incorporate relevant needs and strategies to overcome barriers. After the training program was finalized, pharmacists were invited to participate in a 2-group pragmatic randomized controlled

ii

trial using a multi-modal recruitment method and randomized to a control (no training) or intervention (training) group. The impact of the training program on pharmacists' knowledge, intention, attitudes, confidence, and perceived barriers regarding naloxone services implementation were assessed via online surveys at baseline, post-training, and 3 months. Self-reported naloxone dispensing behaviors (structure activities, process activities, number of naloxone prescriptions dispensed) were measured at baseline and 3 months. Mean differences between control and intervention groups across time-points were assessed using mixed ANOVA and adjusted analyses were conducted using generalized estimating equations (GEE) with negative binomial distribution. Factors motivating adoption/implementation of naloxone services were assessed to inform future strategies for increasing program uptake.

Results and Implications: Interviews found that, although pharmacists were generally supportive of community pharmacy-based naloxone services, they were uncomfortable approaching and communicating with patients regarding opioid overdose risk and the need for naloxone. Perceived patient resistance, perceived high cost of naloxone for patients, and lack of time were also major barriers to community pharmacy-based naloxone services implementation in Alabama. Experts recommended creating a normative culture of safety in the pharmacy by utilizing safety-centered marketing and communication strategies, using a universal (time-efficient) rather than targeted (time-intensive) approach to recommend naloxone, and "closing the loop" by following up with both patients and providers after naloxone provision. The EmpoweringCommunityPharmacists training program was created based on these findings and delivered as a live webinar in 2018-2019.

From pre- to post-training, there was a statistically significant increase in Alabama community pharmacists' mean intention score (5.35 to 6.10, p=0.023) and confidence score

(5.52 to 6.16, p<0.0005) for providing naloxone services among the intervention group. These changes in intention and confidence were statistically significant compared to control (intention p=0.014, confidence p=0.016) and were maintained at 3 months. There was no statistically significant change in pharmacists' knowledge, attitudes, or perceived barriers from pre- to post-intervention among intervention compared to control. Compared to control, there was no difference in the number of naloxone service structure activities completed, process activities engaged in, or naloxone prescriptions dispensed in the intervention group. At baseline, pharmacists were most motivated by social gains.

Results suggest that this training program, created using a participatory design approach, effectively increases intention and confidence to adopt/implement naloxone services among community pharmacists. Future studies should focus on leveraging pharmacists' motivation to provide naloxone services by fostering a sense of professional fulfillment. Study outcomes are expected to inform adoption/adaptation of the training program in other states.

Acknowledgements

Table of Contents

List of Tables

List of Figures

List of Abbreviations

ADPH   Alabama Department of Public Health

ALBME   Alabama Board of Medical Examiners

CDC   Centers for Disease Control and Prevention

DAST-10   Drug Abuse Screening Test 10

DEA   Drug Enforcement Administration

EMS   Emergency Medical Services

ISD   Individuals with Substance Use Disorder

MAT   Medication-Assisted Treatment

NIDA   National Institute on Drug Abuse

ONDCP   Office of National Drug Control Policy

OOPP   Opioid Overdose Prevention Program

OTP   Opioid Use Treatment Program

OUD   Opioid Use Disorder

PBSS   Prescription Behavior Surveillance System

PDMP   Prescription Drug Monitoring Program

RIOSORD   Risk Index for Overdose or Serious Opioid-Induced Respiratory Depression

SAMHSA   Substance Abuse and Mental Health Services Administration

SBIRT   Screening, Brief Intervention, and Referral to Treatment

SUD   Substance Use Disorder

THN   Take-Home Naloxone

Chapter 1. Introduction

Overview of the Study

Despite new laws allowing pharmacists to dispense naloxone without a physician's prescription, community pharmacists in Alabama miss opportunities to dispense naloxone to at-risk patients. Educational programs targeted to pharmacists' specific needs have the potential to decrease these missed opportunities and prevent opioid overdose-related deaths. Thus, the **purpose** of this project is to create and assess a targeted pharmacist training program for naloxone therapy management in order to increase community pharmacists' knowledge, attitudes, confidence, intention, and dispensing of naloxone for prevention of opioid overdose deaths. A naloxone training program was be created using a **participatory design approach** that incorporates pharmacists' needs and expert strategies to overcome barriers. The effectiveness of the program was evaluated in terms of pharmacists' knowledge, attitudes, confidence, intention, and naloxone dispensing behaviors at baseline, post-training, and 3 months using a two-group pragmatic randomized controlled trial. Factors motivating adoption/implementation of pharmacy-based naloxone services were also be assessed to inform future strategies for increasing program uptake.

Background and Significance

Opioid abuse is a major public health issue in the United States

Over 250 million prescriptions for opioid pain relievers were written in the U.S. in 2012,[1] and almost two million people were non-medically dependent on these medications in 2014. Indeed, prescription methadone, hydrocodone, & oxycodone are commonly implicated in

medication-related fatalities.[2] Nearly 22,000 people in the U.S. die annually due to prescription opioid overdose,[2] as many as 62 people daily.[1,3,4] The state of Alabama is of particular concern, as it has the highest rate of opioid prescribing in the U.S.,[5] & drug overdose deaths increased 20% from 2013-2015.[6] However, as of 2012, only 14,500 opioid addiction treatment centers were registered in the U.S.,[7] with only 188 qualified physicians in Alabama.[8] One of this study's goals is thus to increase the number of trained providers, particularly community pharmacists, who can serve as a valuable source of information about opioid risks and overdose death prevention, as well as a point of referral to needed patient services.

Community pharmacists can help alleviate the problem of opioid overdose deaths by dispensing naloxone to high-risk opioid users

Naloxone is a fast-acting, non-addictive prescription medication used to reverse opioid overdose.[9] Studies show that patients taking high doses of opioids ($\geq$ 50 mg of morphine equivalents daily) are especially vulnerable to overdose deaths,[10] but co-dispensing of naloxone with chronic opioid prescriptions can reduce opioid-related emergency-department visits by 63%.[11] Thus, access to naloxone is critical for these high-risk patients. Since 2015, all 50 states, including Alabama, have passed bills allowing pharmacists to dispense intranasal or intramuscular naloxone to patients for opioid overdose prevention without a physician's prescription.[2,12-16] Taking into account the fact that over 60,000 pharmacies exist in the United States (nearly four times the number of opioid addiction treatment centers), as well as pharmacies' extended hours of operation and no need for appointments,[17] using community pharmacists as an opioid prevention resource has the potential to reach a large number of patients, especially patients that do not see a physician regularly.[18] Thus, it is crucial that

pharmacists understand how to dispense naloxone according to their state's policies. One of this study's goals is to increase pharmacists' knowledge and skills to dispense naloxone to patients at high risk of opioid overdose.

Pharmacists are inadequately trained to implement new naloxone policies

In fact, few pharmacists utilize the prescriptive authority granted by new policies.[2] Misinformation about naloxone,[19] as well as inadequate pharmacist training regarding stocking, counseling, and billing of naloxone are cited as major barriers to pharmacy naloxone dispensing in the United States.[11,20] Difficulty identifying or relating to high-risk patients poses an additional barrier.[19,21] However, differences in naloxone prescribing laws by state make identification of relevant barriers and formation of a training program targeted to end-users' needs problematic.[16] Previous naloxone training programs through the American Pharmacists Association,[22] Substance Abuse and Mental Health Services Administration,[23] and schools of pharmacy[24] were not tailored to overcome pharmacists' self-reported barriers and address their self-reported training needs at the state level, especially in Alabama. Indeed, little is known about Alabama pharmacists' training needs. Thus, one goal of this study is to assess state-specific training needs & barriers regarding pharmacy-based naloxone service adoption/implementation in order to provide relevant education to pharmacists in Alabama.

Problem Statement and Purpose of the Study

A training program incorporating end users' needs via a participatory design approach may empower pharmacists to dispense naloxone

Educational programs incorporating stakeholders' needs using a participatory approach are more effective at changing behavior compared to programs that do not incorporate end-users' needs.[25-28] However, pharmacists' individualized needs have not been incorporated into naloxone training in Alabama thus far.[22-24] Incorporating these needs would increase the training's relevancy & feasibility.[25-28] **Accordingly, the purpose of this study is to create and assess the effectiveness of a pharmacist training program for naloxone therapy management in order to increase community pharmacists' knowledge, attitudes, confidence, intention, and naloxone dispensing activities for prevention of opioid overdose deaths.** A naloxone training program was created using a participatory design approach that incorporates pharmacists' needs and expert strategies to overcome barriers. The effectiveness of the program was evaluated in terms of pharmacists' knowledge, attitudes, confidence, intention, and naloxone dispensing behaviors at baseline, post-training, and 3 months using a two-group pragmatic randomized controlled trial (RCT) design in Alabama. Factors motivating adoption/implementation of pharmacy-based naloxone services were also be assessed. The specific aims of the study are outlined below.

Specific Aims

Specific Aim 1: To incorporate community pharmacists' training needs and experts' strategies to overcome barriers regarding pharmacy-based naloxone services implementation into the development of a targeted training program in Alabama

First, semi-structured telephone interviews with community pharmacists and opioid abuse experts were used to identify pharmacists' naloxone training needs (format and content) and barriers. Second, qualitative analysis was conducted and the results were used to inform the

development of the training program, using a participatory design with a panel of pharmacists and experts to incorporate relevant needs and strategies to overcome barriers.

Depending on the results of interviews and stakeholder panel feedback, potential planned training formats included an online, webinar, in-person, paper-based, or combination of formats. Based upon the authors' previous research, paper-based or online was the anticipated preferred CE format, with a length of 1 to 3 hours.[29,30] Training topics also depended on interview and panel findings, but potential topics included: naloxone stocking and billing; patient counseling tips and talking points; product demonstration skills; strategies for approaching prescribers regarding naloxone prescriptions; strategies for identifying, approaching, and communicating with at-risk patients; strategies for co-prescribing of naloxone with chronic opioid prescriptions; and pharmacy-based naloxone services implementation checklists or guidelines.[31,32] Based on findings from interviews, the final training program used a live online webinar format and contained 3 modules: 1) naloxone basics and Alabama legalities; 2) naloxone service implementation strategies; and communication strategies.

Specific Aim 2: To evaluate a targeted naloxone training program among community pharmacists in Alabama

This aim was conducted using a pragmatic two-group randomized controlled design and assessed using quantitative methodology. After the training program was finalized in Aim 1, pharmacists were invited to participate in Aim 2 using a multi-modal email and mailed recruitment method and randomized to a control (no training) or intervention (training) group. The impact of the training program on pharmacists' knowledge, perceived barriers, attitudes, confidence, and intention to dispense naloxone was assessed via pre-post online surveys at

baseline, post-training, and 3 months. Self-reported naloxone dispensing behaviors were

measured at baseline and 3 months. Mean differences between control and intervention groups

across time-points were assessed using mixed ANOVA. Factors motivating

adoption/implementation of naloxone services were also assessed to inform future strategies for

increasing program uptake.

Expected Contributions and Implications

We expected to find that participating community pharmacists' knowledge, confidence,

and number of dispensed naloxone prescriptions increased, suggesting that training programs

created using a participatory design approach were an effective method to involve Alabama

pharmacists in opioid overdose death prevention strategies. This work will: 1) have a broad

impact on patient care and public health; 2) improve pharmacy practice; and 3) add to the

organizational adoption/implementation literature. The outcomes of this study are expected to

inform adoption or adaptation of the training program in other states.

First, this study is expected to have a broad impact on patient care and public health.

Given the high rate of opioid overdose deaths in the U.S. (over 10 per 100,000), especially in the

southern and northeastern states, methods to prevent these deaths are sorely needed.[4,33,34] The

state of Alabama is of particular concern, as it has the highest opioid prescribing rate in the

country, but lacks a sufficient number of specialized opioid abuse treatment facilities and

specially trained physicians.[7,8,35] Thus, by training community pharmacists to dispense naloxone

to their full capacity, we will increase the number of providers who are capable of educating the

public about opioid risks and providing services for patients using opioids, increase patient

access to naloxone, and potentially prevent opioid overdose deaths.

Second, this study has the potential to improve pharmacy practice. Pharmacists have successfully adopted/implemented clinical care services such as immunizations and medication therapy management (MTM).[36-46] However, their role in substance abuse treatment and overdose death prevention has been limited.[47] By creating a targeted training program to increase pharmacists' knowledge, confidence, and ability to dispense naloxone and overcome adoption/implementation barriers, we will advance the role of the pharmacist. This will potentially open up new practice areas for pharmacists and may increase pharmacy revenue streams and job satisfaction, thus improving not only patient care but also the profession of pharmacy.

Third, the results of this study will add to the organizational adoption/implementation literature. Currently, there is limited research regarding factors motivating community pharmacists' adoption or implementation of naloxone services.[48] Understanding of these factors will help to increase future program uptake and aid in adaptation of the program in other states. Furthermore, by assessing the impact of a targeted training program on implementation of naloxone services structure and process indicators, we will gain further insight into strategies to overcome barriers and increase the extent of pharmacy-based naloxone services implementation at the organizational level.

Innovation

The concept of using pharmacists as a key component to reduce opioid abuse is innovative

Pharmacists are very accessible healthcare professionals in both urban and rural locations; indeed, there are nearly four times as many pharmacies in the United States compared to opioid addiction treatment centers.[7] Furthermore, due to the walk-in nature and extended

hours of community pharmacies, pharmacists are able to serve in-need patients after-hours, or patients who do not regularly see a provider for care.[49] Previous research also shows that pharmacists are willing to assist in opioid-dependence treatment.[21] However, although recent laws allow pharmacists to dispense naloxone without a physician's prescription, misinformation about naloxone deters them from doing so.[19] Therefore, training pharmacists to dispense naloxone is feasible and will increase access to naloxone compared to current medical practice.

The study's approach is also unprecedented

There is a lack of studies among community pharmacists in regards to their self-reported naloxone training preferences, factors affecting adoption/implementation of naloxone dispensing practices according to state policies, and the impact of training programs on pharmacists' beliefs and behaviors.[22-24] Previous naloxone training programs through the American Pharmacists Association,[22] Substance Abuse and Mental Health Services Administration,[23] and schools of pharmacy[24] were not tailored to overcome pharmacists' self-reported barriers and address their self-reported training needs. The proposed training program differs from others in that it will incorporate Alabama pharmacists' heretofore unknown self-reported training needs. This will be accomplished using a participatory design approach to elicit pharmacists' feedback during training program development. This type of approach is shown to increase accessibility and usefulness of training, as well as end-users' motivation to participate.[27,28] This study will also investigate factors motivating adoption/implementation of pharmacy-based naloxone services, which may inform changes in existing training programs in order to increase pharmacist buy-in.

Organization of Dissertation

This dissertation is organized into several parts. A review of the literature follows in Chapter 2, which will provide more background regarding the state of opioid abuse and misuse in the United States, the specific problems faced in Alabama, as well as the neurobiological basis for addiction and associated treatments and preventive measures, particularly naloxone. The role of the pharmacist is expounded upon, with emphasis on recent laws and lessons learned from pharmacy-based Medication Therapy Management (MTM) services adoption and implementation. Lastly, we will review pertinent theories that inform the foundation of this study, especially the Consolidated Framework for Implementation Research (CFIR) and Motivations for Adopting Innovation model, with additional elements taken from the Theory of Planned Behavior.

Chapter 3 will explain the methods associated with Aims 1 and 2, including our research questions or hypotheses, research design, inclusion and exclusion criteria, recruitment strategies, measures and data collection, data analysis, expected findings, and known limitations. Chapter 4 reports the results of Aims 1 and 2 of the study according to the research questions and hypotheses put forth in Chapter 3. Finally, the dissertation ends with a discussion of the study findings, implications, recommendations and conclusions in Chapter 5.

Chapter 2. Literature Review

Introduction

Given the rising problem of prescription drug abuse & high number of opioid-related deaths annually in the United States, mechanisms to distribute naloxone (a fast-acting opioid reversal agent) are sorely needed. Therefore, this study aims to increase community pharmacists' awareness, knowledge, and confidence in dispensing naloxone (an opioid overdose reversal agent), with the ultimate goal to increase patient access to naloxone and help prevent opioid overdose deaths. In order to lay a foundation for this study, the following sections in this chapter will review the state of opioid abuse and misuse in the United States, the specific problems faced in Alabama, as well as the neurobiological basis for addiction and associated treatments and preventive measures, particularly naloxone. The role of the pharmacist is expounded upon, with emphasis on recent laws and lessons learned from pharmacy-based Medication Therapy Management (MTM) services adoption and implementation. Lastly, we will review pertinent theories that inform the foundation of this study, especially the Consolidated Framework for Implementation Research (CFIR) and Motivations for Adopting Innovation model, with additional elements taken from the Theory of Planned Behavior.

The Opioid Epidemic in the United States

The number of drug overdose deaths in the United States is at an all-time high.[3] In 2015, over 60% of these overdose deaths were attributed to opioid drugs,[3,50] quadruple the amount from 1999.[3] Indeed, over 33,000 people in the U.S. die annually due to opioid overdose,[2,33] as many as 91 people daily.[1,3] In 2015, deaths due to any opioid reached over 10 per 100,000 throughout the United States,[4] with the increasing trend in overdose deaths most severe in the

southern (4.4 per 100,000) and northeastern (3.6 per 100,000) regions.[33,34] Contributing to this

rash of opioid overdose deaths are a recent increase in deaths due to non-prescription opioids, as

well as a continually high number of deaths due to prescription opioids.[4,50]

Non-prescription opioid abuse

Non-prescription opioid abuse is on the rise.[3] Drugs falling under the non-prescription

opioid category include illegal opioids like heroin, as well as illegally manufactured synthetic

opioids.[3] In regards to heroin use, there has been a steady increase from 2002 to 2013, including

increases in addiction as well as instances of new use.[3,51] Addiction is especially prevalent in

non-Hispanic white males living in urban areas.[51,52] This upward trend in heroin use and

addiction may be caused in part by a trifecta of reasons, including greater availability, decreased

price, and higher heroin purity.[3,53,54] Indeed, heroin trafficking across the border in the

Southwestern U.S. increased markedly in the past few years.[3,55] All this led to almost 13,000

overdose deaths due to heroin in 2015, representing a tripling in heroin overdose deaths from

2010 to 2015.[3,50]

Another type of non-prescription opioid refers to synthetic opioid drugs that are

manufactured via illegal means and not obtained via prescription diversion, most notably

fentanyl and fentanyl derivatives.[3] As of 2015, the rate of overdose deaths due to synthetic

opioids (other than methadone) was 3.1 per 100,000 in the United States,[56] with 9,500 overdose

deaths in 2015.[50,57] Overdose deaths attributed to these drugs rose almost 60% from 2014 to

2015, and a shocking 219% from 2010 to 2015,[56] with illicitly manufactured fentanyl (IMF)

making up the bulk of cases.[3,56] In fact, a dangerous trend has been noted in the U.S. regarding

fentanyl, with illegally manufactured batches often "adulterated" with heroin or cocaine,

increasing the overdose-potential of this illicit narcotic.[3] These trends regarding synthetic

opioids are most severe in the Midwest, northeast, and southern areas of the U.S., with fatal

overdoses due to IMF more concentrated east of the Mississippi River.[56] In particular, Ohio and

Virginia experienced a rapid increase in IMF seizures by law enforcement from 2010 to 2015.[56]

Prescription opioid abuse

Non-prescription opioid-related deaths are not the only concern; prescription opioid

abuse is a major cause of the continued rise in opioid overdose deaths.[3] Almost two million

people were non-medically dependent on prescription opioids in 2014, and as of 2015, nearly

22,000 people in the U.S. die annually due to prescription opioid overdose,[2] as many as 62

people daily.[1,3,4] Almost 50% of deaths due to opioid overdose were caused by prescription

opioids,[58] and 75% of heroin users abuse prescription opioids prior to starting heroin.[3,59]

Furthermore, up to 25% of people prescribed opioids on a chronic basis become addicted.[58]

Once addicted, users of prescription opioids are forty times more likely to become addicted to

heroin, greatly increasing their chances of a fatal overdose or debilitating injection-related

infection such as Hepatitis C or Human Immunodeficiency Virus (HIV).[52] As such, prescription

opioid abuse is a prime target for treatment/prevention and intervention strategies. Methadone,

oxycodone, and hydrocodone are commonly abused prescription opioids, and lead to the most

overdose deaths due to prescription opioids.[58] In recent years, abuse and diversion of

pharmaceutical (legally manufactured) fentanyl has also become an increasing problem.[57]

Risk factors and underlying causes contributing to the opioid epidemic

Trends in prescription opioid abuse are difficult to explain, as there is no clear correlation between usage and the prevalent diagnoses in any geographic area.[58,60] However, there are several risk factors that may increase the likelihood of opioid abuse, addiction, and/or overdose in individuals, including: "Dr. shopping," or using more than one physician or pharmacy to get similar opioid prescriptions;[61-64] using a high daily dose of opioid analgesics (over 90 morphine milligram equivalents (MME) daily);[63,65-68] having low income;[69] or living in a rural area.[58,69] Furthermore, those with a history of substance abuse or psychological ailment are at increased risk of opioid abuse.[58,70,71] Certain prescription combinations also put patients at increased risk of overdose, including simultaneous prescribing of opioid analgesics with benzodiazepines (a class of anxiolytics or sedatives), as well as prescribing of extended release opioid formulations for the treatment of short-term pain.[58,61]

There are several other underlying factors that contribute to this opioid epidemic, including overprescribing of opioid analgesics and increasing access to diverted and illegal opioids.[3,72,73] Regarding overprescribing, over 250 million prescriptions for opioid analgesics were written in the U.S. in 2012[1] – this number is enough for everyone in the U.S. to have a prescription.[58] In fact, the number of opioid prescriptions increased almost four-fold in a period of fifteen years from 1999 to 2015.[3] Likewise, pharmacy, hospital, and clinic purchases of prescription opioid medications increased four-fold from 1999 to 2010.[3,74] Interestingly, inappropriate opioid prescribing seems to be higher amongst members of the U.S. Medicaid population, with higher doses, opioid-benzodiazepine combinations, and multiple simultaneous opioid analgesic prescriptions in 40% of Medicaid patients' claims in 2010.[58,61] However, it is

unclear if the need for increased opioid prescriptions was justified since there was not a corresponding increase in pain diagnoses in the U.S. during this time period.[3,75,76]

Regarding access to diverted prescription opioids, the majority of people unlawfully obtain prescription opioids from a friend or relative either by buying them, stealing them, or even for free.[77] However, diversion of prescription opioids (the transfer of legal opioids to an illegal market) can occur through various channels, including theft from pharmacies or clinics, prescription forgery,[72] inadvertent prescribing by a legitimate medical provider to an illegitimate patient, or purposeful prescribing by a medical provider to an illegitimate patient (these clinics are referred to as "pill mills").[78] In fact, there were a staggering 3,405 pharmacy robberies across the entire U.S. between 2014 and 2016, the majority of which involved the theft of controlled substances, including prescription opioids.[79] These diverted prescription opioids may be sold to others for exorbitant amounts, with oxycodone having a street value as high as $1.00 per milligram, meaning that a ninety-count prescription of Percocet® 10/325mg could cost as much as $900 on the street.[80]

Access to illegal opioids is also growing, with trafficking by land across the Mexican border making up the majority of heroin entering the United States.[73] In addition, counterfeit prescription pills imported from outside the U.S. have been noted with increasing frequency in the last several years, often manufactured with fatal doses of fentanyl.[81,82] Synthetic opioids and precursor chemicals often come into the U.S. overseas from China, with counterfeit pills or IMF crossing into the U.S. from Canada or, more often, Mexico.[82] Once in the U.S., there are eight main "drug corridors" through which illegal drugs are transported, with movement east or north from the Mexican border or west and north from Florida or the Gulf Coast.[55] This is important, as rising prescription opioid prices and increasing prescribing regulations (discussed in more

detail in a later section) force individuals to switch from prescription opioid use to cheaper, more accessible illegal opioids, increasing the chance of a fatal overdose.[3,52,59]

The Opioid Epidemic in Alabama

The state of Alabama is of particular concern, as it has the highest rate of opioid prescribing in the U.S.,[5] and drug overdose deaths increased 20% from 2013-2015.[6] In 2016, the rate of opioid prescribing throughout the U.S. was 66.5 prescriptions per 100 people, while in Alabama the rate was double the national rate (121 prescriptions per 100 people).[35] In certain counties in Alabama, the rate was even higher, exceeding 235 prescriptions per 100 people in Walker County alone.[35] In fact, the rate of prescribing in Alabama is three-fold higher than in Hawaii, the state that prescribes the least opioids.[58] In 2015, the rate of drug overdose (not specific to opioids) in Alabama was 15.7 per 100,000, compared to 16.3 per 100,000 throughout the entire United States.[68] Although the rate of drug overdose deaths in Alabama is below that of West Virginia, the state with the highest rate of overdose deaths (41.5 per 100.000),[33] the high rate of opioid prescribing in Alabama has severe implications regarding future increases in prescription opioid overdose rates in this state. In particular, the rate of drug overdose deaths attributed to opioids was 4.7 per 100,000 in the state of Alabama in 2015,[83] but much higher in certain counties – 15.4 per 100,000 in Jefferson County,[83] compared to 10.4 throughout the entire Unites States.[68] Focusing on Jefferson County, heroin-related deaths were high yet trending downwards in 2015 and fentanyl-related deaths were trending upwards, with prescription opioid overdose making up a large percentage (34%) of all medication-related deaths.[84] From 2015 to 2016 alone, the number of fentanyl-related deaths in Jefferson County increased by over 200%, with hydrocodone, oxycodone, and methadone making up the highest number of other

15

prescription opioid-related overdose deaths.[85] Of particular note, Alabama differs from other

states in that the majority of opioid overdose deaths occur in urban areas (Jefferson County, for

example), whereas other states have experienced a problem more in rural areas.[58,69,84,86] In this

case, it is critical to address the opioid abuse and overdose problem in Alabama, especially in

these high-risk populous areas, before it becomes even worse. Given the high likelihood of

prescription opioid abuse to lead to future heroin use, a focus on prescription opioid abuse and

overdose prevention makes sense as a first step in Alabama.[52]

Not only are opioid prescribing and overdose death rates of concern in Alabama, but

access to diverted and illegal opioids is also a concern. From 2014 to 2016, there were almost

200 pharmacy robberies in the state of Alabama alone,[79] with prescription opioids such as

oxycodone common targets.[87] Furthermore, the state of Alabama is bordered by three of the

eight major drug trafficking corridors in the United States (Corridors A, F, and G), making the

potential for future increases in opioid abuse and overdose death quite high.[55] Thus, the need for

proactive prevention strategies in Alabama is critical.

Etiology of Opioid Abuse and Addiction

We will need to understand the categories of opioid drugs in order to better understand

the patterns of opioid abuse and misuse in the United States. Opioid drugs available by

prescription may also be referred to as "opioid analgesics," and are intended to treat moderate to

severe pain, including cancer pain.[88] These are schedule II-IV drugs in the United States and

include: natural opioid analgesics, such as morphine and codeine; semi-synthetic opioid

analgesics, like oxycodone, hydrocodone, and hydromorphone; and synthetic opioid analgesics,

including methadone, tramadol, and fentanyl.[88] Non-prescription opioid drugs are manufactured

16

illicitly, and include illegal opioids (often Schedule I) such as heroin, which is derived from morphine but is 2-4 times more potent.[80,88-90] Heroin is highly addictive, and may be injected, snorted, or smoked.[52] Non-prescription opioids also include illegally manufactured (outside of legal pharmaceutical companies) synthetic opioids, such as fentanyl and carfentanyl (used by veterinarians to tranquilize large animals).[88,91] These two drugs are 50-100 and 10,000 times more potent than morphine, respectively.[88,91]

Inappropriate use of these prescription or non-prescription opioids falls along a spectrum from misuse or non-medical use to dependence and addiction.[80,88] Opioid misuse or non-medical use refers to using prescription opioids without a valid prescription for oneself (for example, using a family members' medication), or using the medication more frequently, for longer duration, or for reasons other than those prescribed.[88] The consequences of opioid misuse may include rapid tolerance (needing to take more of the drug to get the same response), physical dependence (not being able to stop taking the drug without entering withdrawal), and/or addiction (at which point the user "craves" the drug and seeks it out).[88,92] At the point of dependence or addiction, this pattern of inappropriate usage is termed "opioid abuse" or "opioid use disorder" (OUD),[80] and is characterized by adverse effects on the user's work, school, social, and/or home life, as well as repeated inability to stop or decrease use.[88] Recent practice is to use the term "individuals with substance disorder" (ISD) to refer to those with OUD, which falls within a broader category of substance use disorder (SUD) composed of those with opioid, alcohol, tobacco, cannabis (marijuana), stimulant, or hallucinogen use disorders.[80,93] Detailed diagnostic criteria for OUD will be discussed in more detail in a later section.

This opioid addiction and abuse can be explained by neuroscience. It comes about due to alterations in brain chemistry with repeated use of opioids.[92] Opioids exert their therapeutic

effect by binding to the mu opioid receptor in the brain, thereby decreasing the sensation of pain but also activating the brain's "reward" system, releasing dopamine and causing euphoria as a side effect.[92] However, repeated exposure to the drug results in decreased sensitivity of the mu opioid receptor as well as up-regulation of nor-epinephrine production, leading to tolerance and physical dependence, respectively.[92] Thus, more and more opioids must be taken to overcome tolerance levels, thereby maintaining the same euphoric effect, and to avoid withdrawal, which is characterized by severe muscle cramps, anxiety, and jitteriness.[92] It is this pleasure-seeking and avoidance of withdrawal that initially drives addiction, eventually becoming a psychological compulsion to use.[92] Even beyond the physical dependence, this psychological aspect may last for years after stopping opioid use,[92] making sustained abstinence difficult and putting the extent of non-prescription and prescription opioid abuse in the U.S. into context. As such, treatment and prevention of opioid use disorder must necessarily be a complicated and multi-faceted process in order to be effective.

Treatment and Prevention Strategies May Help to Minimize the Opioid Abuse Problem

Treatment and prevention of opioid abuse has become a priority of the Unites States federal government in recent years. In fact, the Obama Administration created the Prescription Drug Abuse Prevention Plan in 2011 and the National Drug Control Strategy in 2014 to promote action.[94] In 2017, President Trump and the Office of National Drug Control Policy (ONDCP) created the President's Commission on Combating Drug Addiction and the Opioid Crisis, recognizing the need for improved prevention strategies and related policies.[95] There are three main areas to target in prevention of opioid overdose deaths, including: 1) improve prescribing and treatment of pain; 2) decrease access to illegal and diverted opioids; and 3) improve or

broaden treatment of opioid use disorder (sometimes referred to as "harm reduction").[3,80] I will discuss each strategy here in order to provide context for the current opioid abuse and overdose prevention landscape in the United States.

Strategies to improve prescribing and treatment of pain

This is an important area of prevention that aims to decrease the number of opioid prescriptions written for patients experiencing chronic non-cancer pain, thus decreasing the risk of addiction, overdose, and diversion of prescription opioids.[96] To this end, various prescribing recommendations have been published, including the Centers for Disease Control and Prevention (CDC) Guideline for Prescribing Opioids for Chronic Pain,[10,96] which discusses alternative treatment options (non-opioid therapy and non-pharmacologic therapy), and safe opioid prescribing practices (dose < 50-90 MME/day, length of treatment no more than 3-7 days for acute pain, avoidance of dangerous drug combinations).[10,97] The Substance Abuse and Mental Health Services Administration (SAMHSA) Opioid Overdose Prevention Toolkit[98] and National Institute on Drug Abuse (NIDA)[99] offer similar recommendations and educational resources for prescribers. Insurance formulary restrictions, manufacturer quantity limits, and restricted pharmacy allotments offer an additional level of control on prescribing practices.[100]

Safe prescribing can be facilitated by the use of states' Prescription Drug Monitoring Programs (PDMPs).[101] The PDMPs are databases of controlled substance prescriptions (Schedule II-V) dispensed to individual patients, and provide a source to monitor and identify misuse or abuse before initiating or continuing a prescription opioid; for example, multiple simultaneous opioid prescriptions from more than one pharmacy or different physicians can alert prescribers to the need for intervention.[101,102] Prescribers (physicians, nurse practitioners,

physician assistants), up to two clinic personnel designated by a provider, pharmacists, representatives of medical and pharmacy certifying and licensing boards, and law enforcement personnel have access to their state PDMPs.[103] However, the effect of PDMP use on prescribing rates is unclear, with studies showing anywhere from a 41% decrease in opioid prescribing[104] to a 9.5% increase after implementation of states' PDMPs.[105] A wide range in the observed effect could be due to variations in the extent of actual PDMP utilization, as only 53% of providers use the database, with the majority citing lack of time as the major barrier to using it, and 22% not even aware it existed.[106]

Although PDMPs exist in all 50 states plus the District of Columbia and providers are mandated by law to check in 38 of those states,[107] variations in laws and limited data sharing across state lines restrict the usefulness of this resource.[108] In Alabama specifically, there is no mandatory training for healthcare professionals before using the PDMP system, although prescribers are mandated to enroll in the PDMP system and check prior to prescribing.[107] There are no enrollment or checking mandates for pharmacists in Alabama, but pharmacies are mandated to report dispensing of a controlled substance as of 2006.[102,107,109] However, the reported dispensing of a controlled substance prescription in Alabama may take up to two weeks to be displayed in the PDMP database; this lag time inhibits real-time checking of the PDMP to aid prescribing.[110] Additionally, Alabama has agreed to participate in interstate data sharing of PDMP information, but full implementation has yet to occur.[102,107] Despite data-sharing limitations of PDMPs at the state level, aggregate PDMP data is useful in informing policy change related to the opioid epidemic.[111] The Prescription Behavior Surveillance System (PBSS) was formed to assist public health officials in monitoring prescribing rates, and currently

uses reports submitted by eight states' PDMPs to create population-based databases that can be used to track changes in prescription opioid abuse before and after policy changes.[111]

Strategies to decrease access to illegal and diverted opioids

Methods to increase enforcement and prevent diversion are important.[94,108] In an effort to prevent prescription opioid diversion, state-level laws regarding prescribing and dispensing regulations may be monitored and enforced by state agencies and regulatory bodies, such as physician or pharmacists licensing boards, as well as law enforcement officers.[94] For example, laws exist in some states limiting the dose and duration (days supply) for which opioids may be prescribed or dispensed, requiring providers to perform specific physical exams prior to prescribing, and regulating pain clinic practices.[112] Furthermore, some states have also passed laws regulating doctor shopping, requiring tamper-resistant prescription forms, and requiring patients to provide identification (a driver's license, etc) when presenting a controlled substance prescription at a pharmacy.[112] In Alabama specifically, pain clinics must be run by a physician licensed in the state of Alabama, and provider compliance with this law is monitored and enforced by the Alabama Board of Medical Examiners.[113] Patients in Alabama may also face jail-time for concealing duplicate opioid prescriptions from a physician.[113]

Additional efforts to prevent prescription opioid diversion include drug take-back programs.[108,114] These programs came about as a result of the Secure and Responsible Drug Disposal Act of 2010 (an amendment to the Controlled Substances Act),[115] and allow patients to safely dispose of expired or unused prescription opioids (or other medications), thus removing the potential for diversion from the home.[114] In fact, hydrocodone, oxycodone, and methadone-containing products made up 32%, 11%, and 5% of all prescriptions returned via drug take-back

21

programs in the Appalachian area of the United States.[116] Drug disposal collection boxes are often located within law enforcement offices,[114] and sometimes pharmacies.[115,117] For example, within 50 miles of Auburn, AL there are 5 pharmacies and hospitals that provide controlled substance disposal services,[118] and within 100 miles there are 10 law enforcement offices.[119] Local law enforcement officers also have the authority to confiscate or destroy suspicious prescription opioids or other suspected diverted controlled substances that they may encounter in the course of their duties.[120] Furthermore, federal, state, and local law enforcement involvement is also key in order to curtail illegal drug trafficking from overseas, Canada, and Mexico.[55] In fact, Governor Bentley formed the Alabama Council on Opioid Abuse and Addiction in 2016 in order to form a collaboration between law enforcement officers, regulators, and healthcare and public health professionals.[117]

Strategies to improve or broaden treatment of opioid use disorder ("harm reduction")

Identification of patients with OUD is a necessary first step in treatment or "harm reduction."[80,121] To this end, the Screening, Brief Intervention, and Referral to Treatment (SBIRT) is a useful tool for identifying, promoting positive behavior change, and referring eligible patients for further treatment.[121] This approach has been shown to significantly reduce the thirty-day incidence rate of illicit drug use over six months by nearly two-fold.[122] Various other screening tools exist as well, including the Drug Abuse Screening Test (DAST-10)[123] and the Risk Index for Overdose or Serious Opioid-Induced Respiratory Depression (RIOSORD).[124] Diagnosis may also be aided by use of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) criteria (ICD-9-CM 304.xx or 305.50; ICD-10 F-11.xx).[80,125] Using this method of diagnosis, a set of eleven criteria are examined (for a complete list of criteria, see Brezing and

Bisaga, 2015),[126] and the presence and/or severity of OUD is determined based on how many criteria are present: the presence of 2-3 criteria indicates mild OUD; 4-5 indicates moderate; and 6 or more indicates severe.[125,126] The CDC Guideline for Prescribing Opioids for Chronic Pain also provides recommendations on how to monitor for misuse, and how to treat patients who develop opioid use disorder.[10,97] Patients may be referred for treatment at a limited number of facilities specializing in opioid addiction; as of 2012, only 14,500 opioid addiction treatment centers were registered in the United States.[7] Patients and providers can identify one of these specialized opioid treatment program facilities using the Substance Abuse and Mental Health Services Administration (SAMHSA) online state-by-state locator.[127] Current treatment can be classified into non-pharmacologic or pharmacologic methods.[128,129]

Non-pharmacologic methods

Non-pharmacologic methods include counseling using approaches such as cognitive-behavioral therapy, contingency management (rewarding positive behavior), or motivational enhancement therapy (gaining commitment to a plan of treatment).[130-132] Peer support groups, as well as treatment through specialized residential, inpatient, or outpatient facilities may also be used to affect behavior change.[130] Treatment facilities may also offer pharmacologic treatment or "detox" for those experiencing withdrawal.[130]

Pharmacologic methods

Pharmacologic methods include use of three main medications: methadone, buprenorphine, and naltrexone.[130] Oral buprenorphine or methadone may be used with a decreasing or "tapering" dose to treat acute withdrawal from opioids,[129] and may also be used for

chronic, maintenance treatment of OUD.[129] Buprenorphine is available in sublingual tablet (Subutex®) and subdermal implant forms,[133] as well as a combination buprenorphine/naloxone sublingual or buccal film (Suboxone®, Bunavail®) and sublingual tablet (Suboxone®, Zubsolv®) for treatment of OUD.[134] Methadone is available as an oral tablet for treatment of OUD.[135] However, due to the partial or full agonistic effects of buprenorphine and methadone at the mu opioid receptor, respectively, they pose a potential for abuse and addiction themselves.[129] This means that buprenorphine and methadone are classified as controlled substances (Schedule III and II, respectively), making their prescription and dispensing more heavily regulated by the Drug Enforcement Administration (DEA).[136,137] Buprenorphine and methadone may be obtained in specialized clinics or treatment facilities, or pharmacies by prescription only.[130] Specialized opioid use treatment programs (OTPs) may offer oral methadone to patients on-site under the supervision of medical staff, or for outpatient treatment by prescription from pharmacies only under limited circumstances; these "methadone clinics" must be certified by the Substance Abuse and Mental Health Administration (SAMHSA) and must meet stringent requirements for staffing and services.[135,138] Furthermore, according to the Drug Addiction Treatment Act (section 823(g) of the Controlled Substances Act), buprenorphine-containing products must be prescribed for outpatient treatment of OUD by providers with specialized training who have applied for and received unique identification numbers (beginning with an "X") from the DEA.[136,137] These providers are also limited by law to treating only 30-100 patients for OUD at a time.[137]

Naltrexone is a mu receptor antagonist and thus poses no risk for addiction, and is available in oral tablet and extended-release injectable formulations with effects lasting twenty-four hours and one month, respectively.[129,139] Similar to buprenorphine and methadone, the oral

form is available in pharmacies by prescription only, but is not classified as a controlled substance and does not require providers to obtain special certification prior to prescribing.[139] As such, naltrexone is ideal for patients who are dedicated to completely stopping opioid use, also referred to as "abstinence."[129,139] It does this by completely blocking the effect of opioids, but is dependent on high levels of adherence from the patient.[139]

Any one treatment may not be enough on its own, however.[140] Medication-assisted treatment (MAT) combines pharmacologic and non-pharmacologic treatment and is the most successful treatment strategy for opioid use disorder.[128,129,132,141] In fact, MAT combining naltrexone and contingency management is shown to reduce the number of patients testing positive for opioid use by 33% compared to pharmacologic treatment alone.[140] Currently, there are 23 specialized treatment programs in Alabama offering MAT,[127] with only 188 physicians in Alabama qualified to treat OUD.[8]

While MAT is an essential component in harm reduction and treating OUD, it is limited to those who seek care from these facilities and providers.[8,127] This potentially leaves other in-need individuals untreated and vulnerable to an opioid overdose. These individuals can still be reached via another important step in harm reduction and overdose death prevention – the use of acute opioid overdose reversal agents, particularly naloxone.[142]

Naloxone is an Effective Opioid Overdose Reversal Agent

Naloxone is a prescription medication used to reverse opioid overdose.[2,12,13] The symptoms of opioid overdose include respiratory depression, pinpoint pupils, slow heartrate (bradycardia), and sedation, and may be fatal.[47] Naloxone works by competitively blocking the mu opioid receptor (a competitive antagonist) to prevent or even reverse the effects of opioids on

the body.[2,12,13] This can be life-saving, especially in the case of reversing respiratory depression.[47] Compared to other medications used to prevent and treat opioid addiction and abuse, namely methadone, buprenorphine, and naltrexone, naloxone has several advantages: it can reverse an opioid overdose after it occurs; it is fast-acting; it has no addiction potential; it is not classified as a controlled substance; physicians do not need a specialized DEA identification number to prescribe it; it is safe for a layperson to administer; and it is available in some states without a prescription.[9,143] This makes naloxone the "drug of choice" for opioid overdose death prevention for "high-risk" patients, especially those who recently stopped using heroin, are in a substance abuse treatment program, or those with risky opioid prescriptions for treatment of pain.[47,144-146] Risky opioid prescriptions may include high dose opioids (>/= 50 MME per day), opioid and benzodiazepine combinations, or use of opioids in those with sleep apnea or other pulmonary conditions.[47,97,144,147] Given the benefits and characteristics of naloxone, convenient access to naloxone in the community setting is vital.[146] In this way, laypeople can prevent opioid overdose deaths in situations unsupervised by medical personnel.[146] Here, I will review: 1) the availability of naloxone in the community setting; 2) outcomes of naloxone access in the community setting; and 3) barriers and facilitators to obtaining naloxone via current common channels.

Availability of naloxone in the community setting: access and dosage forms

Naloxone is ideal for acute use in the community setting. Besides being carried by first responders such as law enforcement and emergency services (EMS) personnel for use in case they are called to the scene of an overdose, naloxone also may be carried by patients or their families/friends/caregivers to use if an overdose should occur.[47] It may be obtained from non-

profit community-based distribution programs (also known as opioid overdose prevention programs (OOPPs) or naloxone take-home programs) via medical staff or non-medical personnel under a physician's protocol – individual patient prescriptions are not needed in this case.[47,146] Recent studies show that the majority of naloxone provision occurs via community distribution programs such as HIV prevention and needle exchange programs, as well as substance abuse treatment facilities like halfway houses or detoxification programs.[47,148] Other sources include methadone programs and various healthcare settings, including medical clinics, hospitals, or emergency departments.[148] It may also be obtained from pharmacies via a physician's prescription, or from pharmacies without a physician's prescription in some states depending on various state laws (discussed in more detail in a later section).[47]

Naloxone was first approved by the FDA in 1971 and is available in several dosage forms which allow for easier distribution and use in those who use opioids, their family/friends/caregivers, and emergency personnel, including: an intramuscular injection vial (0.4 mg/mL) with syringe or prefilled syringe (2mg/2mL) plus a mucosal atomizer device for intranasal administration, otherwise known as a "naloxone kit"; an auto-injector (Evzio®, 0.4mg/actuation) recently approved in 2014; and a nasal spray (Narcan®, 2mg or 4mg/actuation) recently approved in 2015.[2,12,13,143,149-151] Naloxone kits may also include other items such as gloves, alcohol wipes, or administration instructions.[152] Although the intramuscular injection and/or prefilled syringe with mucosal atomizer device (MAD) are the most affordable options, they have several limitations: the conversion of the pre-filled syringe to an intranasal dosage form with the MAD is not FDA-approved (it is an off-label use of the naloxone injection); and complicated assembly poses problems for quick administration.[47,153] On the other hand, the auto-injector walks the administrator through the process using voice directions, and can even be

administered through clothing (similar to an Epi-pen for anaphylaxis).[47] The hidden needle on

this device also makes it patient-friendly.[47] The nasal spray is also very patient-friendly, with a

simple-to-use one-spray delivery with no assembly.[47] Naloxone's fast onset of action (five to six

minutes for intramuscular or subcutaneous injections, or eight to thirteen minutes for intranasal

administration) and short duration of action of 20 to 90 minutes also makes it useful for non-

medically trained individuals who may not have immediate access to care or emergency medical

services (EMS), especially in rural areas.[154,155]

Outcomes of naloxone access in the community setting

Distribution of naloxone in the community shows positive outcomes in terms of

preventing overdose deaths.[156] In fact, distribution of naloxone in the community setting may

decrease opioid overdose deaths by as much as 46%, with distribution of naloxone to 164 people

needed to prevent one death.[47,157] Studies show that immediate survival after opioid overdose

and subsequent naloxone administration ranges from 83% to 100%,[158] with the odds of recovery

over 8 times higher for those who were administered naloxone by a bystander versus those who

were not.[159] Naloxone is administered by an opioid user's family member 20% of the time,[148]

and is associated with few adverse events, the most common being symptoms of opioid

withdrawal (tachycardia or fast heartrate, irritability, trembling, abdominal cramps, and

nausea/vomiting).[143,158] Of note, however, recipients may become combative after overdose

reversal with naloxone due to quickly bringing on symptoms of opioid withdrawal,[117,143] with a

systematic review reporting various arrests and confrontations with first responders post-

naloxone administraiton.[158] To initiate or maintain overdose reversal, however, several doses of

naloxone (0.4 to 2mg, depending on dosage form) may be required every two to three minutes

28

(up to a maximum of 10 mg).[143] Also, community-based training regarding naloxone

administration and opioid overdose prevention is shown to increase individuals' knowledge and

confidence regarding what to do in the case of an overdose and how to correctly administer

naloxone.[158-164] Not only that, but community distribution of naloxone to laypeople is cost-

effective from a societal perspective, with an incremental cost-effectiveness ration (ICER) of

$438 per quality-adjusted life-year (QALY).[47,165]

Barriers and facilitators to obtaining naloxone via current common channels

Cost and limited access may be a barrier to naloxone acquisition for some opioid users or

healthcare and law enforcement facilities/personnel.[47] Although not FDA-approved, intranasal

naloxone kits with injectable naloxone and mucosal atomizers are the most affordable at around

$50.[47] The Narcan nasal spray and Evzio auto-injector are not available in generic forms as of

yet, and cost around $125 and $3,750 at full retail price, respectively.[47] Medicaid does cover

naloxone, but other commercial insurance payers may not, depending upon the plan.[117] Some

manufacturer discount programs do exist to aid with the cost, such as Adapt Pharma's discounted

Public Interest Price, which offers Narcan nasal spray for $75 to members of the U.S.

Communities Purchasing Alliance, including law enforcement, EMS, and community-based

organizations.[147] Kaleo (the manufacturer of Evzio) also offers the auto-injector to non-profit

distribution organizations for free via their Product Donation Grants, and also offers a Patient

Assistance Program.[156,166]

Community distribution programs or OOPPs such as the Save One Life Program through

the University of Alabama at Birmingham,[167] substance abuse treatment programs, and

state/local public health departments provide a low-cost option for some patients.[142,146]

However, the supply through such programs is limited and not accessible for all patients due to finite number and poor geographic spread of these facilities.[146] In 2014, approximately 140 community, state, or local organizations provided naloxone distribution programs or OOPPs (some multi-site), but nearly 30% of these programs had trouble consistently obtaining and stocking naloxone, and over 50% lacked resources to effectively distribute naloxone kits to a broader population.[146,158] Furthermore, such distribution programs do not reach in-need prescription opioid users as frequently as heroin users.[146] Thus, there is a gap in naloxone provision to prescription opioid users, necessitating further studies in this area.[146]

Pharmacists Have a Critical Role in Opioid Overdose Death Prevention Strategies

Alternative means of access to naloxone and naloxone training for patients using prescription opioids is critical.[146,154] Patients taking high doses of opioids ($\geq$ 50 mg of morphine equivalents daily) are especially vulnerable to overdose deaths,[10] but co-prescribing and co-dispensing of naloxone with chronic opioid prescriptions can reduce opioid-related emergency-department visits by 63%.[11] Thus, access to naloxone is vital for these high-risk patients. Given this fact, methods to increase co-prescribing and co-dispensing of naloxone with risky opioid prescriptions make sense.[11] However, methods to increase co-prescribing via traditional prescribers (physicians, nurse practitioners, etc) in clinic settings are limited by the relatively few number of qualified treatment centers and specialized providers; as of 2012, only 14,500 opioid addiction treatment centers were registered in the U.S.,[7] with only 188 qualified physicians in Alabama.[8] In the treatment programs that do exist, space and resources are limited.[117] Therefore, there is a need to increase the number of trained providers in the community who provide a means of access to naloxone and are able to educate patients on its proper use.

Community pharmacists represent one such provider due to: 1) greater access to naloxone compared to traditional providers; 2) recent laws increasing pharmacists' ability to distribute naloxone in the community setting; and 3) successful implementation of other pharmacy-based clinical services.[2,12-17,36-43]

Community pharmacies provide greater access to naloxone compared to traditional providers

Pharmacists are well-positioned to significantly contribute to opioid abuse and overdose death prevention in the community setting. Taking into account the fact that over 60,000 pharmacies exist in the United States (nearly four times the number of opioid addiction treatment centers), as well as pharmacies' extended hours of operation and no need for appointments,[17] using community pharmacists as an opioid prevention resource has the potential to reach a large number of patients, especially patients that do not see a physician regularly, need care after-hours, or are taking risky opioid prescriptions readily identified during pharmacists' medication review.[18] In Alabama in particular, there are only 23 clinics and facilities offering specialized opioid treatment programs,[127] compared to 1,282 community pharmacies,[168] representing an opportunity for pharmacists to supplement naloxone access in areas without access to a specialized treatment program. Thus, it is crucial that pharmacists understand how to dispense naloxone according to their state's policies.

Recent laws increase pharmacists' ability to distribute naloxone in the community setting

Laws regarding naloxone dispensing in community pharmacies vary by state.[2,12-16,169] Since 2015, all 50 states, including Alabama, plus the District of Columbia have passed bills allowing pharmacists to dispense intranasal or intramuscular naloxone to patients for opioid

overdose prevention without a physician's prescription.[2,12-16,169] Of the 50 states plus D.C., four

states have passed laws allowing pharmacists to dispense naloxone without any prescription at

all (either physician or third-party/pharmacist initiated); 14 via pharmacist-initiated prescribing;

and thirty-three (including Alabama) via a statewide standing order or other standing order.[16]

Thirty-seven states also have policies protecting someone who administers naloxone to an

individual in good faith ("Good Samaritan" laws), with some states providing all immunities,

while others provide civil and criminal immunity only (including Alabama), professional

immunity only, or other combinations.[169,170] Additionally, thirty-four states (including Alabama)

require by law that the individual being dispensed naloxone receive training or instruction on

how to use it.[170] This means that community pharmacists in these states must be properly

educated and able to counsel and demonstrate naloxone use.[170]

In fact, within Alabama, the House Bill HB208 first passed on June 12, 2015 allowing

pharmacists to dispense naloxone via a statewide standing order, and also protecting pharmacists

from civil and criminal liability for doing so.[171] This standing order (SO) was most recently

renewed by Scott Harris, MD, the Acting State Health Officer, on March 8, 2018 and expires

upon the date when and if naloxone becomes an over the counter medication.[171] The details of

the Alabama law code (Ala. Code § 20-2-280)[171] allow pharmacists to dispense

intramuscular/subcutaneous or intranasal naloxone to: an opioid user at risk of overdose; family,

friends, or caregivers of someone at risk for opioid overdose; and first responders such as

members of a fire department or law enforcement.[2,12,13,171] There are five specific actions that a

pharmacist in Alabama must perform when dispensing naloxone according to the SO

(paraphrased):[171]

    1) Train the recipient on how to recognize an opioid overdose and to call 911;

2) Dispense naloxone and explain its use to the recipient;

3) Counsel the recipient on resources for addiction treatment;

4) Have recipient sign the client contact form documenting training was received; and

5) Keep a record of everyone who has received naloxone via this standing order.

From this, it is seen that the naloxone dispensing process is multifaceted, and that community pharmacists not only must know how to identify, communicate with, and dispense naloxone to eligible patients, but also serve as a source of referral for patients to treatment facilities.[171] Thus, pharmacist training and understanding regarding the many steps involved in the SO is critical to increase community pharmacy-based naloxone distribution.

Adoption and Implementation of Pharmacy-Based Naloxone Services

Early adopters of pharmacy-based naloxone services have been successful.[47] Rhode Island and Massachusetts were some of the first states to adopt pharmacy naloxone services, and individuals with substance use disorder (ISDs) and pharmacists have expressed satisfaction with and desire for continued naloxone access via community pharmacies.[48] Several trend-setting pharmacies in Boston, Seattle, and Pittsburgh have also successfully incorporated identification of patients who are eligible for naloxone into their workflow by: 1) checking for high-risk opioid prescriptions during the dispensing and medication profile review process; 2) proactively screening patients for signs of opioid abuse or high-risk behaviors, such as screening for participation in methadone clinics or needle-exchange programs; or 3) forming a collaborative relationship with physicians who refer eligible patients to the pharmacy for naloxone.[2] In fact, the Kelly-Ross Pharmacy Group in Washington State partnered with the Seattle Department of Public Health and University of Washington Alcohol and Drug Abuse Institute to provide

naloxone kits via a Take-Home Naloxone (THN) program.[172] Furthermore, a novel system to

track pharmacy-based naloxone dispensing has been developed in New Mexico (the first state to

allow pharmacists to prescribe naloxone) through a partnership between the University of New

Mexico and the New Mexico Pharmacists Association.[86] Pharmacists report their

prescribing/dispensing of naloxone to this system, called the Prevention of Opioid Overdose by

New Mexico Pharmacists (POINt-Rx) Registry.[86] Between 2013 and 2016, 133 pharmacist-

prescribed naloxone kits were reported to the registry, with 56.4% of prescriptions initiated at the

request of the patient, and 43.6% initiated due to risky opioid prescriptions or history of opioid

abuse/misuse upon pharmacist medication review.[86]

Community pharmacists are not dispensing naloxone to their full capacity

Although these early adopters of pharmacy-based naloxone services showed success,

adoption and implementation remain low overall.[2,86,173,174] For example, only 45% of

pharmacies in Massachusetts stock and dispense naloxone,[175] 30% of pharmacists in Kentucky

are unwilling to implement naloxone dispensing,[176] and only 11.3% of pharmacy-based naloxone

dispensing in New Mexico occurs in rural areas, presenting a gap in access that needs to be

addressed.[86] Nationwide, naloxone dispensing in pharmacies increased from 463 per quarter in

2010-2013 to 4,291 prescriptions per quarter in 2015, demonstrating some uptake of new

pharmacy-based naloxone services.[47,177] However, given the 60,000 community pharmacies in

the U.S., annual dispensing of naloxone totaled less than one prescription per pharmacy per

year.[17,47,177] Considering the 33,000 people in the U.S. that die annually due to opioid overdose,

there is still a large population of ISDs unreached.[2,33] Furthermore, in pharmacies that do

dispense naloxone, few pharmacists utilize the prescriptive authority granted by new policies,[2]

with the majority of naloxone dispensed in community pharmacies originating through a primary care physician's prescription.[47,177] While this collaboration with primary care physicians is positive, it represents missed opportunities for pharmacists to utilize new laws to help hard-to-reach patients that do not seek or do not have access to traditional care.[47] Additionally, only 11.3% of pharmacy-based naloxone dispensing occurs in rural areas, presenting a gap in access that needs to be addressed.[86]

In Alabama specifically, adoption and implementation of naloxone services in community pharmacies is lacking, with pharmacist involvement more prevalent in centrally located public health departments.[178] For example, the Jefferson County Department of Health implemented a pharmacist-led naloxone prescribing service in 2014, with 150 naloxone kits dispensed; however, a 131% increase in prescription opioid-related deaths from 2014-2015 indicates the need for additional measures to increase uptake in community pharmacies in Alabama and extend the reach of pharmacy-based naloxone services.[179,180] Corporately-owned CVS and Walgreens pharmacies in Alabama (and other states) have also adopted naloxone services, but information regarding the extent of implementation is limited.[181]

Barriers and facilitators to pharmacy-based naloxone services adoption and implementation

Identification of barriers to pharmacist dispensing of naloxone may help to explain these missed opportunities and gaps. However, research on barriers to community pharmacist dispensing/prescribing of naloxone is limited. Among the research that exists, misinformation about naloxone,[19] as well as confusion regarding stocking, counseling, & billing of naloxone[11,20,182] are cited as major barriers to effective naloxone dispensing in community pharmacies. Difficulty identifying or relating to high-risk patients poses an additional barrier, as

well as perceived high cost of the medication.[19,21] Furthermore, barriers to naloxone dispensing

may differ across states, since naloxone distribution laws vary by state.[16,21] However, little is

known about state-specific barriers to dispensing in community pharmacies, particularly in

Alabama; without this knowledge, targeted strategies to overcome these barriers cannot be

developed. Additionally, information is especially limited regarding barriers and facilitators to

pharmacy-based naloxone dispensing services adoption and implementation decisions.[21] Written

and telephone surveys with pharmacists and technicians in New York, Virginia, Illinois, Florida,

Texas, California, and Washington revealed that pharmacists & technicians are willing to

participate in opioid harm reduction strategies.[21] This willingness is a key component to

individual and organizational readiness to change, but may vary by state, pharmacy type, and

urban/rural setting.[180] Thus, factors leading to adoption and implementation of pharmacy-based

naloxone dispensing services need to be better understood.

Strategies to overcome barriers to pharmacy-based naloxone services implementation

Few studies have addressed the need for strategies to overcome barriers for implementing

pharmacy-based naloxone services.[48] Among existing studies, several interventions have proved

useful in increasing pharmacist naloxone dispensing, including academic detailing, opt-out

strategies, social marketing, the influence of authority figures, and pharmacist training

programs.[48,178,183-185] In particular, education and training via academic detailing in the Veterans

Affairs (VA) system showed promise, with a 7-fold increase in naloxone provision two years-

post intervention.[183] Multi-pronged pharmacist training and public social marketing campaigns

in New Mexico were also useful, with Medicaid claims for naloxone prescriptions increasing 9-

fold two years after implementation began.[184] Other multi-pronged strategies, like that taken by

the Walgreens Corporation RE-AIM Program, used pharmacist training plus the influence of authority figures (corporate policy), to influence the adoption of naloxone services in pharmacies; Walgreens now offers these services in 33 states.[185] Pharmacist training via the Washington State Take-Home Naloxone (THN) Program also resulted in a reported 99 naloxone kits dispensed and 20 opioid overdose reversals via one pharmacy.[178] Thus, the potential impact of pharmacist training on naloxone services implementation and patient outcomes can be seen.[178] The next section will examine existing naloxone training programs in more detail in order to better understand why community pharmacists are not dispensing naloxone to their full capacity.

Naloxone Training Programs for Community Pharmacists

Despite current programs and resources, pharmacists are not adequately trained to confidently identify and counsel eligible patients regarding naloxone, overcome personal and organizational barriers, and implement naloxone dispensing services in the community pharmacy setting.[48,176,182,186] In fact, a study in West Virginia showed that only 20.4% of community pharmacists feel comfortable selling naloxone without a prescription, pointing to inadequate training and preparation.[173] Similar studies in other states also showed that pharmacists lack confidence in their ability to identify eligible patients and counsel patients regarding naloxone, with 75% believing that their training was insufficient.[176,187] This points to the need for targeted, relevant, and feasible training programs for pharmacists.[16,21] Some states (New Mexico and New York, for example) have recognized the need to train pharmacists about naloxone and require pharmacists to complete specific training before they can prescribe/provide naloxone.[188] While having a required training program is beneficial in terms of its standardization across the state,

little is known about whether such training would adequately prepare pharmacists in a way that they would be ready and equipped to engage in naloxone counseling.

Existing naloxone training programs

Examination of current naloxone training programs may help to explain why pharmacists lack confidence in providing naloxone. Multiple resources exist to aid community-based non-profit, state, or local public organizations to implement naloxone distribution programs and train patients and first responders (law enforcement and EMS personnel).[156] These general, non-pharmacy specific naloxone training programs and resources include the National Institute on Drug Abuse (NIDA) web page,[189] Project DAWN (Death Avoided with Naloxone) through the Ohio Department of Health,[190] the Substance Abuse and Mental Health Services Administration (SAMSHA) Opioid Overdose Toolkit,[23] U.S. Department of Justice (DOJ) Law Enforcement Naloxone Toolkit,[191] the Veterans Affairs Opioid Overdose Education and Naloxone Distribution (OEND) program,[192] and others (Table 2.1). However, there are limited resources and implementation guides specifically for community pharmacists.[156] Current pharmacy-specific programs, training, and resources exist in some early adopter states, often through collaboration with state chapters of the American Pharmacists Association (APhA) or schools of pharmacy, including: the California Pharmacists Association (CPhA) continuing education (CE) training;[22] the Illinois state opioid antagonist training program in partnership with the Illinois Pharmacists Association (IPhA);[193] the New Mexico RPh Rx Authority and A Dose of Reality training programs in partnership with the University of New Mexico and the New Mexico Pharmacists Association;[184] and others (Table 2.2). The StopOverdose.org website[194] and Kelly-Ross Pharmacy Group Naloxone Toolkit[32] provide resources for providers, first responders,

pharmacists, and patients in Washington state, while the Prescribe to Prevent website offers

resources for providers, pharmacists, and patients that are not state-specific, with pharmacist CE

through the University of Rhode Island College of Pharmacy.[195,196]

The most common content in existing training programs includes: how to

recognize/respond to an overdose; and naloxone formulations/administration.[22,196-201]

Continuing education credit is offered for some programs but not all, ranging from 0.75 to 7.00

credits, and program format consists of online webinars, in-person training, and provision of

online articles and video resources.[22,196-201] As we can see in Tables 2.1 and 2.2, there is no

uniformity of content, with some few programs including additional items such as discussion of

patient counseling tips, where to find naloxone, or explanation of state-wide standing

orders.[22,196-201] This makes it difficult for pharmacists to find a comprehensive guide to naloxone

services implementation. Furthermore, important elements are missing from these training

programs, pointing to several areas for improvement in order to increase community

pharmacists' willingness to adopt/implement naloxone services.

Table 2.1. Existing General Naloxone Training Programs

Program	Location & Sponsors	Target Audience	Content	Format	CE Credit
Multi-Component Audience Not Including Pharmacists					
A Primer on the Opioid Morbidity and Mortality Crisis: What Every Prescriber Should Know[200]	National - American Medical Association (AMA) Opioid Task Force	Physicians, nurse practitioners, physician assistants	- Factors putting patients at risk for opioid abuse or overdose - Opioid prescribing guidelines - Overview of opioid-related harm reduction strategies (including naloxone) - Links to more article and video resources from other sites are available at the AMA End the Epidemic website[202]	Knowledge-based online webinar	0.75 (Physician CME)
National Institute on Drug Abuse (NIDA)[189]	Federal	Anyone	- Naloxone formulations & how to use - Where to find naloxone	Online articles & video resources	0
Project DAWN (Death Avoided with Naloxone)[190]	Ohio - Ohio Dept of Health	Public health & community distribution organizations (including pharmacies)	- How to recognize/respond to an overdose - Naloxone formulations & how to use - Billing Medicaid - Documentation templates	Online articles and form resources	0
Substance Abuse and Mental Health Services Administration (SAMSHA) Opioid Overdose Toolkit[23]	Federal	Anyone (community members, first responders, prescribers, patients & family members, people in recovery)	- How to recognize/respond to an overdose - Naloxone formulations & how to use - Provider billing (CPT codes) - Websites with more information for patients	Online articles and links to external physician CE programs	0
U.S. Department of Justice (DOJ) Law Enforcement Naloxone Toolkit[191]	Federal	Law enforcement personnel	- Naloxone formulations & how to use - Documentation templates	Online articles, forms, & video resources	0
National Safety Council (NSC) Prescription	National	Patients & community members	- General information about naloxone	Online articles, in-person training	0

Drug Community Action Kit[203]					
Harm Reduction Coalition (HRC)[156,204]	National, with state subsidiaries: - Drug Overdose Prevention & Education (DOPE) Project: San Francisco - New York SKOOP (Skills & Knowledge on Overdose Prevention)	Anyone (especially patients & community distribution programs)	- Best-practice guidelines for community distribution programs - How to recognize/respond to an overdose - Naloxone formulations & how to use	Online articles, forms, & video resources, in-person training	0
Project Lazarus[205]	North Carolina	Providers, patients	- How to recognize/respond to an overdose - Naloxone formulations & how to use - Documentation templates - Provider billing (CPT codes) - Patient education handouts	Online articles and form resources, in-person training	0
Pathways to Safer Opioid Use program[199]	Federal	Healthcare & public health professionals (including pharmacists)	- How to communicate with patients - How to recognize at-risk individuals - How to collaborate interprofessionally	Online interactive video (role-play scenarios)	1 (Physician CME)
Veterans Affairs Opioid Overdose Education and Naloxone Distribution (OEND) program[192,206,207]	Federal - Veterans Affairs Administration	Providers, patients	- How to recognize/respond to an overdose - Naloxone formulations & how to use	Online articles & video resources, in-person training	0
Revive![208]	Virginia - Virginia Department of Behavioral Health and Developmental Services (DBHDS)	Health professionals, patients (lay rescuers)	- How to recognize/respond to an overdose - Naloxone formulations & how to use	Online articles & video resources, in-person training	0

	- Virginia Department of Health - Virginia Department of Health Professions				
West Virginia Harm Reduction Program[209]	West Virginia - Marshall University School of Pharmacy - Cabell Huntington Health Department	Anyone (especially patients)	- How to recognize/respond to an overdose - Naloxone formulations & how to use	In-person training	0
Massachusetts Department of Public Health Overdose Education and Naloxone Distribution (OEND) Program[210]	Massachusetts - Massachusetts Department of Public Health	Anyone (patients, family members, community members, state agencies, first responder organizations, providers)	- How to recognize/respond to an overdose - Naloxone formulations & how to use - Staff training and organizational service delivery guidelines - Where to find naloxone	Online articles, in-person training	0
Naloxone and Overdose Prevention Education Program (NOPE-RI)[196,198]	Rhode Island	Health professionals, non-medical volunteers	- How to recognize/respond to an overdose - Naloxone formulations & how to use - Where to find naloxone	Online articles & video resources, in-person training	1.25 (Physician & pharmacist)
OverdoseFreePA[211]	Pennsylvania - University of Pittsburgh School of Pharmacy	Anyone (friends & family, health professionals, public safety professionals, persons using opioids, people in recovery)	- Naloxone formulations & how to use - Where to find naloxone	Online articles & video resources	0
Multi-Component Audience Including Pharmacists					
Collaborating to Combat Misuse and Abuse of Illicit and Prescription Drugs in	Alabama (Huntsville & Montgomery) - Auburn University	Pharmacists, physicians, nurses practitioners, physician assistants,	- General facts about opioid and substance abuse - Naloxone formulations & how to use	In-person conference	7

Alabama: An Interprofessional Conference[201]	Harrison School of Pharmacy - AL Department of Public Health (ADPH) - AL Department of Economic & Community Affairs (ADECA)	RNs, dentists, veterinarians, social workers, law enforcement, patients, community members	- How to use the Prescription Drug Monitoring Program (PDMP) - Professional roles in treating & preventing opioid misuse & abuse		
Putting Naloxone Into Action![212]	National - College of Psychiatric and Neurologic Pharmacists	Pharmacists, providers,	- Naloxone service models - Patient education points - Naloxone billing - Strategies to overcome naloxone services implementation barriers	Online webinar	1
Prescribe to Prevent: Overdose Prevention and Naloxone Rescue Kits for Prescribers and Pharmacists[195,196]	National - Pharmacist CE through University of Rhode Island College of Pharmacy - Physician CE through Boston University School of Medicine	Pharmacists, providers, patients	- Naloxone formulations & how to use - Prescribing protocols - Patient counseling information & handouts - Naloxone billing & stocking - Collaborative practice models (pharmacy "success stories")	Online articles & video resources, plus home-study online CE course with video-simulated patient encounters	1.25
StopOverdose.org[194]	Washington state	Pharmacists, providers, patients, first responders	- Factors putting patients at risk for opioid overdose - How to recognize/respond to an overdose - Naloxone formulations & how to use - Billing of naloxone - Collaborative drug therapy agreement forms - Implementation checklist for pharmacies - Marketing materials (flyers & posters)	Online articles & video resources	0

| Kelly-Ross Pharmacy Group Naloxone Toolkit[32] | Washington state | Pharmacists, providers, patients | - Factors putting patients at risk for opioid overdose
- How to recognize/respond to an overdose
- Naloxone formulations & how to use
- How to stock naloxone
- Provider billing (CPT codes)
- Prescribing protocols
- Collaborative drug therapy agreement forms
- Implementation guide for pharmacies | Online articles & video resources | 0 |

Table 2.2. Existing Pharmacist-Specific Naloxone Training Programs

Program	Location & Sponsors	Target Audience	Content	Format	CE Credit
Opioid Overdose Education & Naloxone Kit Distribution (OEND) training at the APA 135th Annual Convention & Tradeshow[181]	Alabama - Alabama Pharmacy Association (APA)	Pharmacists	- How to recognize/respond to an overdose - Naloxone formulations & how to use - Examples of established OEND programs - Naloxone standing order in Alabama - General tips for implementing an OEND program (1 PowerPoint slide)	In-person CE course	1
American Pharmacists Association (APhA) Opioid Use, Abuse and Misuse Resource Center[213]	National - American Pharmacists Association (APhA)	Pharmacists	- Opioid prescribing & other clinical guidelines - Naloxone access laws by state - Current opioid news - Collection linking to other trainings	Online articles & video resources	0
Best Practices for Overdose and Naloxone Education in Higher Education[214]	National - American Association of Colleges of Pharmacy (AACP) Substance Abuse Education & Assistance SIG	Pharmacists	- Best practices in overdose & naloxone education in the pharmacy curricula	Online live webinar	0
Naloxone: Fundamentals for Pharmacists Dispensing to Caregivers and Patients at Risk for Opiate and Opioid Toxicity[22]	California - California Pharmacists Association (CPhA)	Pharmacists	- Factors putting patients at risk for opioid overdose - How to recognize/respond to an overdose - Naloxone formulations & how to use	Knowledge-based home-study online CE course	2
Illinois State Opioid Antagonist Training Program[193]	Illinois - Illinois Pharmacists Association (IphA)	Pharmacists	- Factors putting patients at risk for opioid overdose - How to recognize/respond to an overdose - Naloxone formulations & how to use - Patient counseling information - Standardized procedures, standing orders, documentation practices - Pharmacy technician & student pharmacist roles	Knowledge-based home-study online webinar	1.75

RPh Rx Authority[184]	New Mexico - University of New Mexico - New Mexico Pharmacists Association	Pharmacists	- Factors putting patients at risk for opioid overdose - Patient screening - How to recognize/respond to an overdose - Naloxone formulations & how to use - Patient counseling information - Prescription ordering information	Knowledge-based in-person or teleconference CE course	2
A Dose of Reality[184]	New Mexico - University of New Mexico - New Mexico Pharmacists Association	Pharmacists, pharmacy technicians, pharmacy clerks, (separate website for patients & community members at https://www.doseofrealitynm.com/)[215]	- How to recognize/respond to an overdose - Naloxone formulations & how to use - Where to find naloxone - Opioid use stigma - Social media & marketing materials (billboards, posters) - Billing for naloxone - Where to refer patients - Patient counseling information	Knowledge-based in-person training with hands-on demonstration	2
Advancing Pharmacy Practice in Kentucky Coalition[216]	Kentucky	Pharmacists	- How to recognize/respond to an overdose - Naloxone formulations & how to use - Standing order & protocols - Billing for naloxone & documentation - Where to refer patients - Patient counseling information & resources	Knowledge-based live in-person and home-study webinar CE course	1.5
Missouri Board of Pharmacy naloxone resource website[217]	Missouri	Pharmacists	- How to recognize/respond to an overdose - Naloxone formulations & how to use - Standing order & protocols - Patient counseling information & resources	Online article resources	0
Dispensing naloxone via a non-patient specific prescription: the role of the community pharmacist[24,218]	New York - University at Buffalo, State University of New York program	Pharmacists	- How to recognize/respond to an overdose - Naloxone formulations & how to use - Standing order & protocols	Knowledge-based home-study webinar CE course	1.5

	- Erie County Department of Health - Harm Reduction Coalition				
State of Connecticut Naloxone Training Program[197]	Connecticut - University of Connecticut School of Pharmacy - Connecticut Pharmacists Association (CPA)	Pharmacists	- Factors putting patients at risk for opioid overdose - How to recognize/respond to an overdose - Naloxone formulations & how to use - Standing order & protocols - Documentation procedures - Patient counseling information & referral resources	Knowledge-based home-study webinar CE course	2

Areas for improvement in existing naloxone training programs

Tailoring to community pharmacists' needs

As a result of the limited understanding of pharmacists' naloxone training needs, existing naloxone training programs may not be tailored to overcome pharmacists' self-reported barriers and address their self-reported training needs. For example, important elements identified by previous studies (Figure 2.1) as key to adoption/implementation of pharmacy-based services are missing from these training programs, including: strategies to build capacity for change; how to identify eligible patients; how to communicate with eligible patients regarding naloxone; and skills-based learning rather than knowledge-based learning only.[32,117,199,216] Detailed and pharmacy-specific guidelines and practical strategies for implementation of key naloxone service components such as marketing, billing, workflow, documentation, and formation of key partnerships is limited.[32,117,199,216] Targeted training materials incorporating these unmet needs may help increase pharmacists' knowledge, confidence, and ability to provide naloxone.[173] In fact, educational programs incorporating stakeholders' needs using a participatory design approach are more effective at changing behavior compared to programs designed without input from end-users.[25-28] Incorporating these needs, as well as building upon a foundation of pertinent theoretical frameworks, would increase the training's relevancy & feasibility.[25-28]

Addressing misconceptions

An important area often left unaddressed by current training programs is stigma against individuals with substance use disorder (ISDs)[219] as well as the belief that distribution of naloxone will prompt individuals to increase their opioid use.[47,220-223] In fact, studies show that the exact opposite is the case – after receiving naloxone and the accompanying counseling, ISDs

more often seek treatment.[47,224-226] Addressing this point in pharmacist training may help pharmacists relate better to ISDs and help to overcome patient-pharmacist interpersonal relationship difficulties that pose a barrier to pharmacy-based naloxone services implementation.[47] Furthermore, regarding the belief that implementing pharmacy naloxone services is too time-consuming, only brief (5-10 minute) education is needed.[227] This brief provision of naloxone education has been shown to increase patients' comfort with using naloxone, ability to use naloxone, and ability to identify someone experiencing an opioid overdose.[227]

Figure 2.1. Facilitators & Barriers to Adoption & Implementation of Pharmacy-Based MTM Services

Facilitators

Individual Factors
- Familiarity with the service
- Positive attitude toward the service

Organizational Factors
Trained pharmacy technicians

Barriers

Individual Factors
- Inadequate training/experience
- Difficulty establishing interprofessional relationships

Organizational Factors
- Difficulties obtaining compensation for services
- Problems with documentation of services
- Lack of adequate staff
- Poor support from management
- Not enough time
- Inadequate access to medical information
- Inadequate facilities/technology

Strategies to Overcome Barriers

Individual Strategies
- Building personal capacity for change
  - Interventions to foster:
    - Proactiveness and employee autonomy
    - Sense of professional fulfillment (desire to help patients, professional duties)

Organizational Strategies
- Building organizational capacity for change
  - Adequate resources
  - Pharmacy technician staffing
- Adapting the service to best fit in the pharmacy workflow
  - Consensus definitions
  - Common service frameworks
  - Billing practices
  - Documentation systems
  - Patient screening protocols
- Building a business model or plan
- Gaining approval or endorsement of decision makers/authority figures
- Finding strategic partners
- Marketing of services

Key Overall Strategy
- Training
  - Knowledge + practical skills

Modifiers

Individual Factors
- Personal interest in the service

Organizational Factors
- Pharmacy type and/or location

Pharmacy-Based Service Adoption & Implementation

Naloxone training programs in Alabama

When looking at Alabama, a state-wide standing order allows pharmacists to dispense naloxone without a prescription; however, there is currently no naloxone training requirement.[188] In fact, in Alabama in particular, few pharmacist- and state-specific training programs exist; there is a particular lack of trainings providing practical strategies to aid implementation (Table 2.2).[181,201] Thus, it is unclear how pharmacists prepare themselves to serve in this capacity. A training, specific to the state requirements and relevant to the needs of pharmacists in Alabama, would be beneficial in facilitating this expanded role of the pharmacist.[25-28] However, at this time, little is known about pharmacists' naloxone training needs in terms of content and format, especially state-specific needs.[228] Limited research suggests that Alabama pharmacists prefer online over in-person training, and over 80% find paper-based CE training very convenient.[30,228] However, no paper-based CE options are currently offered, even though pharmacists find this format convenient.[30] Given the lack of comprehensive and need-specific training and implementation guidelines in Alabama, this represents a prime target for intervention to increase adoption/implementation of pharmacy-based naloxone services in Alabama.[32] Therefore, we will next examine successfully implemented pharmacy services to learn practical strategies for implementation that may be incorporated into training programs.

Adoption and Implementation of More Established Pharmacy Services: Models for Pharmacy-Based Naloxone Services Implementation

Given the limited literature on pharmacists' naloxone dispensing and counseling, we will consult other, more established pharmacy-based services to better understand facilitators and barriers related to individual decisions and the organizational environment (Figure 2.1).[44,229,230]

Successful implementation of other pharmacy-based clinical services

Pharmacist dispensing of naloxone is not unprecedented. This is only one of the many advances in clinical pharmacy practice in recent years, and pharmacists have demonstrated their ability to successfully implement new clinical services in the areas of immunizations[36-40] and medication therapy management (MTM).[41-46] Indeed, implementation of these community pharmacy-based services improves patient access to care, with pharmacy influenza immunization services reaching those who do not see a provider regularly (up to 25% of pharmacy vaccine recipients), and also patients who were at high risk of complications (almost 50% of pharmacy customers).[36] Patient outcomes are also improved by pharmacy-based services, with pharmacist MTM shown to decrease hospitalizations[43] and decrease healthcare expenditures by over $3,000 per person with appropriate management of medications.[41] In recent years, pharmacists in some states have also been granted prescribing authority; for example, the SB 493 bill in California in 2014 allowed pharmacists to prescribe birth control, preventive travel medicine, and nicotine replacement products under their own authority.[231] With additional training and certification (Advanced Practice Pharmacist Certification), pharmacists are also allowed to adjust certain patient prescription therapy and order laboratory tests under this bill.[231] The high patient satisfaction (over 90%) with such services bodes well for the successful implementation and eventual routinization of pharmacy-based naloxone dispensing services.[36,180] Examination of facilitators, barriers, and strategies used to overcome barriers of these successfully implemented pharmacy services will help us to understand how to increase adoption and implementation of naloxone services in community pharmacies (Figure 2.1).

Facilitators and barriers to pharmacy-based MTM services adoption and implementation

Using community pharmacy-based Medication Therapy Management (MTM) services as an example, pharmacist familiarity with Medicare Part D MTM services and a positive attitude regarding the benefit of MTM services for patients were cited as facilitators to adoption and implementation (Figure 2.1).[230,232] The level of these individual factors (personal characteristics) influenced the extent of implementation, with pharmacists who were more familiar with Medicare Part D MTM services or with a more positive attitude regarding MTM benefits being more likely to contract with an MTM software platform compared to those who were less familiar or had a less positive attitude.[232] Help from trained pharmacy technicians was also cited as a facilitator to MTM services implementation.[233]

On the other hand, multiple barriers prohibited implementation of pharmacy MTM services, including: difficulties obtaining compensation for services; problems with documentation of services; difficulty establishing interprofessional relationships; lack of adequate staff; poor support from management; not enough time; inadequate access to medical information; inadequate facilities/technology; and inadequate training/experience (Figure 2.1).[46,186,233-236] Individual factors influenced the impact of these implementation barriers, namely pharmacist interest in pursuing MTM; those who were more personally interested in the service were more likely to rate lack of staff and inadequate access to medical information as barriers compared to those who were less interested.[234] Pharmacists who did not receive compensation for MTM services were also more likely to rate poor support from management, difficulties obtaining compensation for services, and problems with documentation of services as barriers to implementation compared to those who did receive compensation.[234] However, not only did individual factors influence implementation, but organizational factors did as well.[234]

Pharmacy type and/or location was shown to influence the perceived impact of implementation barriers, with pharmacists practicing in community settings more likely to rate problems with documentation of services and difficulty establishing interprofessional relationships as barriers to MTM services implementation compared to those practicing in non-community settings.[234] Furthermore, even if pharmacists are ready, willing, and able to provide MTM services, this may not be enough to overcome barriers such as difficulties obtaining compensation for services and problems with documentation of services.[186,234] Additional help may be needed to overcome barriers, which may be provided in the form of interventional studies or targeted training programs.[186,235]

Strategies to overcome barriers to pharmacy-based MTM services implementation

Although studies regarding strategies to overcome barriers to pharmacy-based naloxone services implementation are limited, additional strategies can be learned by examining established pharmacy MTM services (Figure 2.1).[229,237] Effective strategies in the MTM services literature include: building personal and organizational capacity for change; adapting the service to best fit in the pharmacy workflow; building a business model or plan; gaining approval or endorsement of decision makers/authority figures; finding strategic partners; and marketing of services.[237,238] For example, pharmacists' and pharmacies' capacity for change can be expanded by interventions targeted to increase personal and organizational characteristics.[237] Personal characteristics of interest include proactiveness and employee autonomy; increasing these perceived factors in pharmacy staff may lead to greater rates of adoption and implementation.[237] Pharmacist adoption of MTM is also shown to result more from a desire to help patients and

fulfill one's professional obligations rather than a desire for compensation; thus, interventions that foster this sense of professional fulfillment may be effective.[235]

To further build capacity for change and promote adoption/implementation of pharmacy MTM services, organizational characteristics such as provision of adequate resources and pharmacy technician staffing have been targeted (Figure 2.1).[237] Adaptation of MTM services to best fit the pharmacy's workflow is also important, including variations of appointment-based, face-to-face, or telephonic services.[235,238] Additionally, partnerships with national or state organizations like pharmacy associations or universities can help to advertise and expand services, as well as other forms of marketing such as newspaper and radio advertisements, website postings, in-store signs or flyers, and academic detailing at physician offices.[235,238] Identification of consensus definitions, common service frameworks, billing practices, documentation systems, and patient screening protocols that can be adapted for implementation at various pharmacies are also important.[235,239-242] Among all these methods, pharmacist training is key to increase service knowledge and practical implementation skills.[235,238] In the next section, we will link these practical strategies learned from MTM to pertinent theoretical frameworks, which will help us to identify key components to target for intervention.

Theoretical Frameworks

By examining key theories in adoption decisions, we can design effective interventions that target individual and organizational characteristics in order to increase adoption and implementation of pharmacy-based naloxone services. From models of pharmacy-based MTM services (Figure 2.1), we saw that strategies to build personal and organizational capacity for change, such as fostering a perception of employee autonomy and adequate technician staffing,

55

were essential in promoting adoption and implementation.[237] This is supported by the

Organizational Readiness for Change model, which states that organization members must be

both willing and able to adopt an innovation.[180] Willingness to adopt/implement a change (in

this case adoption or implementation of naloxone services) is influenced by individuals' and

organization members' knowledge and how they value the service.[180] Perceived ability to

adopt/implement the change depends on individuals' absorptive capacity (ability to learn or try

something new) and organization members' task demands, resource availability, and situational

factors.[180] Particular factors may be targeted in interventions to increase this readiness to

change, especially elements from two key theories: 1) Kennedy and Fiss' Motivations for

Adopting Innovation Model; and 2) the Consolidated Framework for Implementation Research

(CFIR). Elements from the Theory of Planned Behavior (TPB) are also informative.

Kennedy and Fiss' Motivations for Adopting Innovation Model

Kennedy and Fiss' Motivations for Adopting Innovation Model helps to explain why

people choose to adopt certain innovations.[243] It originates from the Classic Two-Stage Model

of Innovation Diffusion, which states that early adopters of an innovation are more motivated by

the desire for economic gains (such as gaining an advantage over competitors), while late

adopters are more motivated by the desire for social legitimacy gains (looking good in front of

one's peers, for example).[180,243,244] Kennedy and Fiss' model expands upon this, postulating that

early adopters are motivated by opportunity framing, such that they seek both economic and

social gains.[243] On the other hand, this model asserts that late adopters are motivated by threat

framing and thus seek to avoid economic and social losses (Figure 2.2).[243] We can leverage the

adoption stage of individuals or organizations (innovators, early adopters, early majority, late

majority, or laggards) in order to target intervention materials and messages to achieve the greatest impact. [180]

We have seen that the naloxone training needs of pharmacists in Alabama are largely unknown,[228] and that pharmacists are not dispensing naloxone to their full capacity.[2,86,173,174] Given that distribution of naloxone to non-healthcare laypeople is a relatively new concept, along with additions to available naloxone dosage forms and the push for pharmacists to dispense naloxone without a physician's prescription, it is safe to assume that the majority of pharmacists in Alabama are at the early adopter stage and will be most strongly motivated by technical or social gains as opposed to losses.[180] If this is the case, the training program messages and materials will be most effective if they are gain framed (opportunity framing) rather than loss framed (threat framing).[243] Thus, it is critical to use a participatory design approach to assess community pharmacists' needs and motivations to adopt naloxone services.[27] Furthermore, once the needs and extent of current naloxone service adoption/implementation are known, examination of the economic and social factors motivating the naloxone service or training program adoption decision will help us to prioritize the strategies found in the MTM literature to overcome individual and organizational barriers.[235,237-242] For example, if a large percentage of community pharmacists in Alabama are motivated by social legitimacy concerns, then naloxone training programs may focus on fostering a sense of professional fulfillment; likewise, if many Alabama pharmacies are motivated by technical efficacy concerns, then training programs may focus on provision of detailed and pharmacy-specific naloxone billing practices.[235,239-243] Therefore, understanding of these motivation factors may inform future strategies for increasing service and training program uptake within Alabama, as well as strategies that can be adapted to increase uptake in other states.

Figure 2.2. Kennedy and Fiss' (2009) Motivations for Adopting Innovation Model[243]

Motivations for Adopting Innovation

Issue Interpretation

	Opportunity	Threat
Technical Efficacy	*Economic Gains*	*Economic Losses*
Social Legitimacy	*Social Gains*	*Social Losses*

Decision Logic

Motivations predicted by the two-stage model (Tolbert & Zucker, 1983)

Early adopters

Late adopters
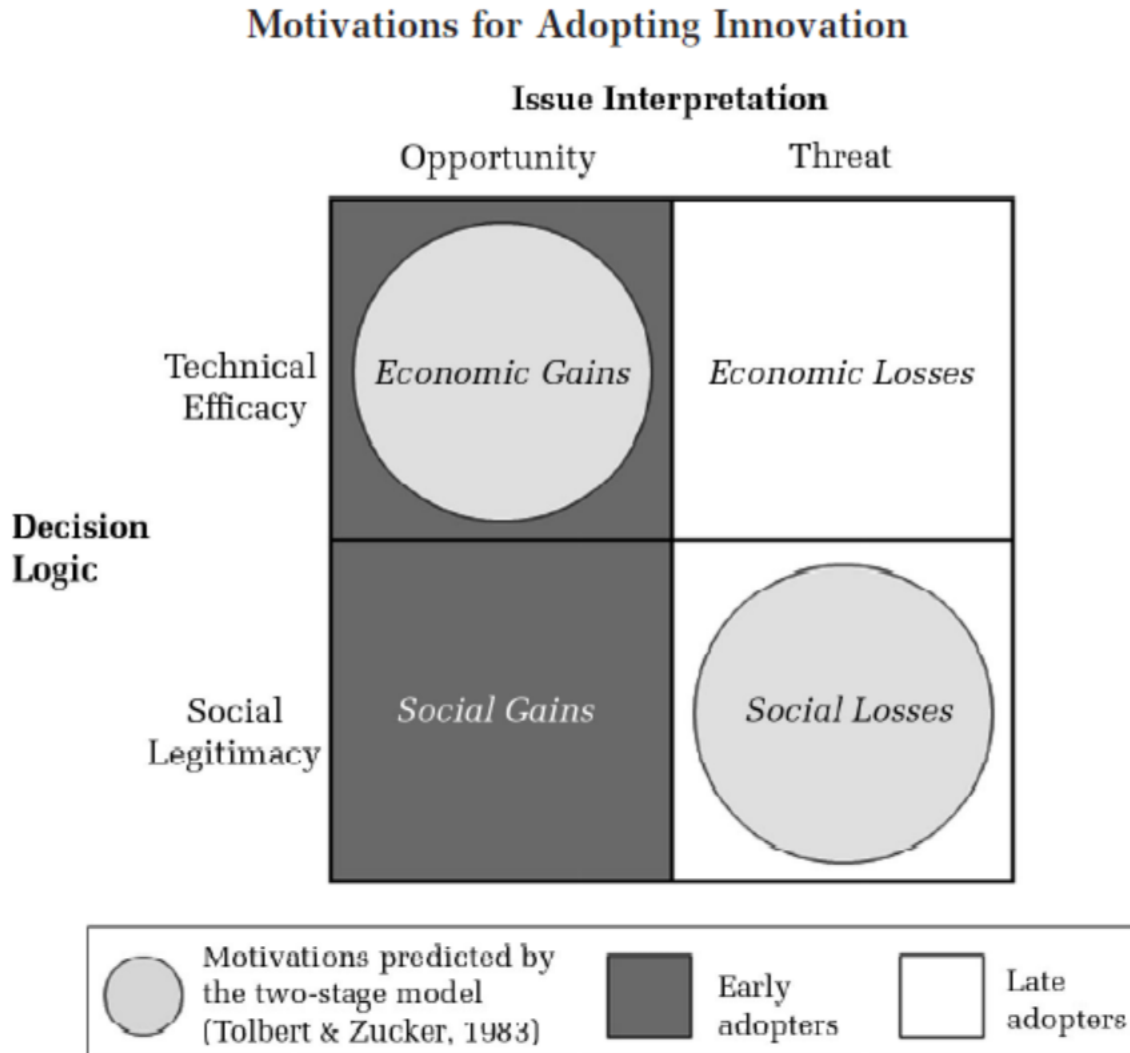
Consolidated Framework for Implementation Research (CFIR)

The Consolidated Framework for Implementation Research (CFIR) includes 5 broad constructs: intervention characteristics; outer setting; inner setting; characteristics of individuals; and process (Table 2.3).[245,246] The intervention characteristics construct includes elements that strengthen an interventions' (pharmacy-based naloxone services') likelihood of being adopted, such as adaptability and cost. The outer setting construct includes elements such as patient needs and peer pressure, while the inner setting incorporates cultural norms and available resources for implementation. On the other hand, characteristics of individuals focuses on elements such as pharmacists' self-efficacy and knowledge. The last construct, process, refers to the method of engaging participants in the intervention and the extent to which the intervention is executed. Optimization of all these factors may result in greater readiness to change and thus greater likelihood to adopt and implement a service innovation.[245,246]

In light of the fact that community pharmacists lack confidence in implementing naloxone services,[176,187] contributing to adoption/implementation below capacity,[2,86,173,174] 4 key components of the CFIR are particularly relevant as targets of intervention, including: pharmacists' knowledge and self-efficacy/confidence in dispensing naloxone, as well as fulfillment of naloxone services structure measures and execution of process measures (Table 2.3).[245,246] Provision of training may increase pharmacists' knowledge and confidence in dispensing naloxone,[176,187] and in turn, the CFIR supports the assertion that increases in these attributes will promote pharmacists' readiness to implement naloxone services.[245,246] Evidence from the MTM literature lends credence to this theoretical viewpoint, as provision of a training program emphasizing the value of pharmacy-based naloxone services and offering practical strategies to address implementation, such as lack of time or difficulty with billing (Figure 2.1),

helped to promote a climate conducive to change.[237,238,245,246] Indeed, the MTM literature

showed that the personal characteristics of pharmacy staff (knowledge, attitudes, and values) and

organizational culture of a pharmacy (norms and values of organization members) may affect

how the service is adapted to fit in the pharmacy workflow.[237,238] Thus, understanding these

personal and organizational factors is essential to affect a successful and sustained

intervention.[180]

Furthermore, the CFIR emphasizes that having necessary structural characteristics and

resources in place increases the likelihood of implementation, while the extent to which service

processes were executed reflects the level of implementation.[245,246] Although the implementation

of naloxone dispensing services is generally below capacity,[2,86,173,174] the MTM literature shows

us that provision of practical strategies to improve service structure resources (staffing,

management support, standard billing procedures) and service processes (screening patients,

finding strategic partners, marketing services) increases pharmacy-based services adoption and

implementation.[235,237-242] Therefore, measurement of structure and process indicators would be

informative regarding the effect of intervention strategies on naloxone dispensing services, and

would help to identify areas for improvement in implementation.

Table 2.3. Consolidated Framework for Implementation Research (CFIR) Constructs[245,246]

Constructs	Components
Intervention Characteristics	Intervention source
	Evidence strength and quality
	Relative advantage
	Adaptability
	Trialability
	Complexity
	Design quality and packaging
	Cost
Outer Setting	Patient needs and resources
	Cosmopolitanism
	Peer pressure
	External policy and incentives
Inner Setting	Structural characteristics
	Networks and communications
	Culture
	Implementation climate
	Readiness for Implementation
Characteristics of Individuals	Knowledge and beliefs about the intervention
	Self-efficacy
	Individual stage of change
	Individual identification with organization
	Other personal attributes
Process	Planning
	Engaging
	Executing
	Reflecting and evaluating

Theory of Planned Behavior (TPB)

Regarding uptake of naloxone services, it takes time to implement behavior change.[247] Therefore, it may be difficult to detect changes in naloxone dispensing behavior in a relatively short period of time.[247] In order to assess the impact of naloxone training programs on pharmacy-based naloxone services implementation, the Theory of Planned Behavior (TPB) tells us that intention to perform naloxone service behaviors (screen patients, dispense naloxone, etc) is also informative.[248] According to the TPB, intention is the greatest predictor of future behavior change; thus, intention may serve as an indicator of likely future implementation.[248] This is important, as changes in pharmacists' intentions can be measured over a much shorter study period compared to changes in pharmacists' actual naloxone service behavior (which may take longer to change), but the intermediate outcome of intention still provides a valuable and meaningful predictor of future implementation and behavior change.[248]

Summary

Opioid abuse and overdose is a major public health issue in the United States.[3] Various treatment and prevention strategies exist, including naloxone, a rapid-acting opioid overdose reversal agent.[2,12,13] Although naloxone is available without a prescription through some public health and non-profit community organizations, the reach of these organizations is limited.[146,158] Thus, in order, to increase access to naloxone for in-need patients at risk of overdose, the number of trained providers needs to be increased.[7,8,117,146] This is particularly critical in Alabama, where the prescribing rate of opioids is the highest in the country.[5,6,35] Given the walk-in and after-hours nature of community pharmacies and recent laws allowing community pharmacists in many states, including Alabama, to dispense naloxone without a physician's prescription, this

presents an opportunity to greatly increase naloxone access.[2,12-18,169]   However, pharmacists are not dispensing naloxone to their full capacity due to individual and organizational barriers, including lack of confidence, unfamiliarity with naloxone services, misconceptions, and difficulties establishing service structure and process components.[2,48,86,173,174,176,186] Strategies from the MTM literature give us insight into successful ways to overcome pharmacy-based service adoption/implementation barriers, chiefly via targeted training incorporating end-users' needs (content and format) via a participatory design approach.[46,186,233-236,238] By linking the strategies learned from the MTM literature to pertinent theoretical frameworks, especially the Kennedy and Fiss' Motivations for Adopting Innovation Model, the CFIR, and the TPB, we can identify relevant components to target for intervention in future studies (Figure 2.3).[243,245,246,248]

Areas needing further study

Thus, in order to facilitate provision of naloxone for opioid overdose prevention in community pharmacies in Alabama and therefore potentially decrease opioid-related deaths, several factors must be understood: pharmacists' naloxone training needs (content and format) and barriers preventing naloxone dispensing; pharmacists' knowledge, attitudes, confidence, and intention to dispense naloxone; and the effect of targeted training developed using a participatory design approach on these attributes and naloxone services adoption/implementation. Factors motivating adoption/implementation of naloxone services should also be examined. This may have a broad impact on the development of innovative new strategies to combat opioid-related deaths, and will inform strategies that may be adapted to increase pharmacy-based naloxone services adoption and implementation in other states.

Figure 2.3. Conceptual Model for Pharmacy-Based Naloxone Services Adoption/Implementation: Incorporating Theoretical Frameworks and Barriers Derived from MTM Programs[46,186,233-236,238,243,245,248]

Organizational Barriers

- Difficulties obtaining compensation for services
- Problems with documentation of services
- Lack of adequate staff
- Poor support from management
- Not enough time
- Inadequate access to medical information
- Inadequate facilities/technology

Individual Barriers

- Unfamiliarity with the service
- Negative attitude toward the service
- Inadequate training/experience
- Difficulty establishing interprofessoinal relationships

Targeted Training Developed Using Participatory Design

- Education
- Skills practice
- Practical strategies to overcome barriers

Change in Attributes

- **Increased:**
- Knowledge
- Attitudes
- Confidence
- Intention
- **Decreased:**
- Perceived barriers

Increased Behaviors

- Naloxone service structure indicators
- Naloxone service process indicators
- Number of naloxone prescriptions dispensed

Adoption Motivations

- **Organizational &/or Individual Factors**
- Technical Efficacy
- Social Legitimacy
- Opportunity Framing
- Threat Framing

CFIR

- **Individual Factors**
- Confidence/self-efficacy
- Value/attitude toward the service
- **Organizational Factors**
- Structure Indicatos
- Process Indicators

TPB

- **Individual Factors**
- Intention

64

Chapter 3. Methods

This dissertation study was conducted using mixed methods. The study is composed of two aims. First, Aim 1 used qualitative interviews with pharmacists and experts to explore Alabama community pharmacists' training needs, attitudes, and barriers regarding dispensing of naloxone for opioid overdose death prevention. Information gained from these interviews informed development of a targeted naloxone training program for community pharmacists. Second, Aim 2 will used quantitative methods to assess the effect of the newly created training program on Alabama community pharmacists' knowledge, attitudes, perceived barriers, confidence, intention, and behaviors regarding pharmacy-based naloxone services. Factors motivating adoption/implementation of naloxone services were also assessed. The research questions or hypotheses, research design, recruitment strategies, measures and data collection, data analyses, expected findings, and limitations are presented separately for each aim in the following sections.

3.1 <u>Specific Aim 1:</u> To incorporate community pharmacists' training needs and experts' strategies to overcome barriers regarding pharmacy-based naloxone services implementation into the development of a targeted training program in Alabama.

3.1.1 Research Question:

This aim sought to explore the following **<u>core research question</u>**:

1. What does adoption/implementation of pharmacy-based naloxone services mean for pharmacists in Alabama?

We focused on **three key domains** of this research question:

    a. Domain 1: What are community pharmacists' experiences with opioid abuse/misuse in their professional roles?

    b. Domain 2: What are community pharmacists' experiences and opinions regarding pharmacy-based naloxone services?

    c. Domain 3: What are community pharmacists' needs and opinions regarding naloxone education/training?

3.1.2 Research Design:

Accordingly, we conducted cross-sectional, semi-structured telephone interviews with community pharmacists and opioid abuse experts in order to elicit desired/necessary naloxone training content and format, as well as attitudes towards and population or state-specific barriers to dispensing of naloxone in community pharmacies. Using a participatory research design and informed by expert opinion, a naloxone training program was developed that incorporates pharmacists' needs and strategies to overcome barriers.

Rationale for research design

This aim was primarily conducted using qualitative research methods. Compared to quantitative methods, a qualitative approach has several advantages (Table 3.1), including the generation of new hypotheses and areas for further study.[249] This is especially advantageous when little is known about the topic under investigation.[249] Furthermore, qualitative methods allow for the discovery of "rich" data; in other words, details may emerge from qualitative methods that researchers may not have thought to ask on a questionnaire, for example.[249,250] As

these studies highlight the "lived experiences" of participants,[251-254] they are often quite persuasive in changing clinical practice,[255] and are typically less expensive than studies using quantitative methods due to the use of a smaller sample size.[249] However, several disadvantages of qualitative compared to quantitative methods must be kept in mind, namely: more time-consuming and labor-intensive data collection and analysis; inability to generalize results to the larger population; and inability to attribute causality to findings.[249,256]

A formative, qualitative methodology was well-suited to this particular aim, as we sought to understand Alabama community pharmacists' heretofore unknown naloxone training needs in terms of content and format.[249] We also sought to explore factors that pose as individual and organizational barriers to adoption/implementation of pharmacy-based naloxone services, which will add to the limited information that is already known. A deeper understanding of these issues will allow us to create a training program that is targeted to end-users' needs, and which may ultimately improve adoption and implementation of pharmacy-based naloxone services in Alabama.

Table 3.1. Advantages and Disadvantages of Qualitative versus Quantitative Methods[249,256]

	Qualitative	**Quantitative**
Advantages	- Smaller sample size - Less expensive - More "rich" data - Can generate hypotheses for further study - Ideal for formative research when little is known about the topic under investigation - Persuasive in changing clinical practice	- Less time-consuming data collection and analyses - Less labor-intensive - Can generalize findings to larger population - Can attribute causality to findings
Disadvantages	- Time-consuming data collection & analysis - Labor-intensive - Cannot generalize findings to larger population - Cannot attribute causality to findings	- Larger sample size required - More expensive - Sacrifice "depth" for "breadth" of findings

3.1.3 Participants and Setting:

Inclusion and exclusion criteria

A sample of community pharmacists in Alabama was studied. Individuals were eligible to participate if they were: a registered pharmacist; and employed (pharmacist-in-charge, staff pharmacist, clinical pharmacist, pharmacy manager, owner) at a community pharmacy located within a priority county in Alabama (Tables 3.2 and 3.3). Only one participant per site was allowed. That is, pharmacists employed at the same community pharmacy as another pharmacist enrolled in the study were excluded from participation for this aim. Pharmacists employed at sites that did not currently stock naloxone could still participate in the study.

Opioid abuse experts within and outside of Alabama were also consulted for this aim to inform development of an evidence-based naloxone training program. Experts were licensed pharmacists, or other medical, public health, or legal professionals (Table 3.2). Experts were eligible to participate if they were at least 19 years of age and were associated with or employed by a pharmacy, medical, public health, or legal organization (Table 3.2), and they had demonstrated experience or substantial knowledge in the areas of opioid abuse, treatment, or harm reduction programs as determined via literature, university or organization websites, or researchers' knowledge of previous contacts[117] (see "Recruitment and procedures" sub-section for more details).

Table 3.2. Aim 1 Inclusion and Exclusion Criteria

	Inclusion	Exclusion
Community Pharmacists	- A registered pharmacist in the state of Alabama - Employed full-time at a retail pharmacy located within a priority county in Alabama - Pharmacist-in-charge - Staff pharmacist - Clinical pharmacist - Pharmacy manager - Owner	Employed at the same community pharmacy as another pharmacist enrolled in the study
	Inclusion	
Experts	≥ 19 years of age - Employed in the U.S. within or outside Alabama - Employed at/as (at least one of the below categories): - Community pharmacy with successfully implemented naloxone services (early adopter) - State or county public health department - Medical examiner's office - College of pharmacy, medicine, or public health - Medical clinic, hospital or substance abuse treatment facility - Community or not-for-profit organization that assists individuals with substance use disorder (ISDs) - District or regional level pharmacy manager, owner, or clinical consultant - A pharmacy, medical, or public health association - A first responder (for example, EMT); - A lawmaker, legal representative, or social worker in the area of substance abuse - Demonstrated experience or substantial knowledge in the areas of opioid abuse, treatment, or harm reduction programs as determined via literature, university or organization websites, or researchers' knowledge of previous contacts[117]	

Sampling frame

In order to recruit pharmacists for whom the proposed study was most relevant and beneficial, community pharmacist participants were sampled from counties in Alabama with the highest opioid death rates. For this purpose, 8 priority counties were selected for use in Aim 1 (3.1.3) and Aim 2 (3.2.3) recruitment (Table 3.3).[83] Data were obtained from the CDC WONDER database[83] from 1999-2015 using ICD-10 codes to identify cause of mortality: X42 (accidental poisoning by and exposure to narcotics and psychodysleptics [hallucinogens], not elsewhere classified); X62 (Intentional self-poisoning by and exposure to narcotics and psychodysleptics [hallucinogens], not elsewhere classified); and Y12 (poisoning by and exposure to narcotics and psychodysleptics [hallucinogens], not elsewhere classified, undetermined intent). Using this database, the precise drug contributing to death cannot be determined. However, on a state-wide level, the CDC WONDER database is the most comprehensive source for county-based vital statistics.[83] The 2013 National Center for Health Statistics (NCHS) Urbanization codes (large central metro, large fringe metro, medium metro, small metro, micropolitan [non-metro], and NonCore [non-metro])[257] were also used to identify rural versus urban counties. The CDC WONDER database provided NCHS Urbanization codes associated with each county. Opioid death rates per 100,000 were calculated using 2015 data, unless death data was suppressed. Number of deaths were suppressed in the CDC WONDER database if there were less than 10 deaths annually in the county. In the case of suppressed values, crude opioid death rates were calculated using aggregated 2013-2015 data. The number of community pharmacies in each county were identified from Hayes Directory, a database containing phone numbers and addresses for pharmacies in the U.S,[168] and are sufficient to meet the sample size

needs for Aims 1 and 2 (3.1.3 and 3.2.3) (Table 3.3). Previous pharmacy collaborators within

counties were also identified in order to purposively target recruitment efforts.

Table 3.3. Priority Counties in Alabama for Aims 1 and 2 Recruitment[a]

County	2013 Urbanization	Crude Death Rate/100,000	No. of Community Pharmacies[b]	No. of Previous Pharmacy Collaborators (Pharmacy Type)
Jefferson	Large Central Metro	15.4	202	15 (Independent), 5 (Chain), 2 (Grocery)
Escambia[c]	NonCore (non-metro)	10.6	11	0
Baldwin	Small Metro	7.9	53	3 (Independent), 2 (Grocery)
Walker[c]	Large Fringe Metro	7.1	29	4 (Independent), 2 (Chain)
Blount[c]	Large Fringe Metro	6.4	8	0
Mobile	Medium Metro	5.8	103	2 (Independent)
Shelby	Large Fringe Metro	5.3	35	2 (Independent), 2 (Chain)
Madison[c]	Medium Metro	1.1	94	5 (Independent), 1 (Chain)
Total in Priority Counties		7.45	**535**	31 (Independent), 10 (Chain), 4 (Grocery)
Total in AL		4.7	1282	36 (Independent), 11 (Chain), 6 (Grocery)
Total in the U.S.		6.8	60,288	

[a]Data obtained from CDC WONDER database[83] for 2015 using ICD-10 codes X42, X62, & Y12 to identify cause of mortality.
[b]The number of community pharmacies in each county were identified from Hayes Directory.
[c]Death rates were compiled from 2013-2015 data, as data for 2015 alone were suppressed in the CDC WONDER database.

Recruitment and procedures

Formative interviews: community pharmacists

Community pharmacists were recruited from these priority counties using a combination

of purposive and snowball sampling beginning with the investigators' contacts from previous

research studies,[40,258] representing a diverse mix of independent versus chain and rural versus

urban pharmacy locations (Table 3.3). Pharmacy/pharmacist contact information was obtained

from Hayes Directory.[168] Recruitment started with previous contacts in Jefferson County (the

county with the highest opioid death rate in Alabama) and continued until all pharmacy contacts

in that county had been exhausted before moving on to contacts in the next priority county.

After all previous contacts had been exhausted throughout all priority counties, other community

pharmacies were invited to participate, beginning in Jefferson County; after the whole list of

community pharmacies was exhausted, we moved on to the next priority county. Recruitment

ended when the point of saturation (when no new information is gained from interviews) had

been reached.[254] We estimated that saturation would be reached after 10 pharmacist interviews

(see "Sample size calculation").[38,259] We started with 5-10 community pharmacists who agreed

to interview, then planned for additional recruitment to be completed if saturation had not been

reached. This method of purposive recruitment has been used successfully by the investigators

in the past,[258] and is more suited to the nature of qualitative inquiry when compared to random

sampling techniques (Table 3.4).

Table 3.4. Advantages and Disadvantages of Purposive versus Random Sampling Techniques[249,254]

	Purposive	**Random**
Advantages	- Commonly used in qualitative vs quantitative studies - Allows for generation of "rich" qualitative data - Less time- and labor-intensive	Can generalize to a larger population (higher external validity)
Disadvantages	Difficult to generalize to a larger population (lower external validity)	- Commonly used in quantitative vs qualitative studies - Sacrifices "depth" for "breadth" of data - More time- and labor-intensive

Formative interviews: experts

Opioid abuse experts were recruited using purposive and snowball sampling from

pharmacist members of the Pain, Palliative Care, and Addiction Special Interest Group (SIG) of

the American Pharmacists Association (APhA); the Substance Abuse Education & Assistance

SIG of the American Association of Colleges of Pharmacy (AACP); faculty at schools of

pharmacy, medicine, or public health identified via literature and university websites; practicing

community pharmacists with opioid prevention program experience as identified via literature;

pharmacy or medical personnel at substance abuse treatment centers or clinics; employees at

departments of public health or medical examiner offices; and investigators' contacts from

previous studies.[117] Recruitment was not to saturation in this case; instead, experts were selected

using a qualitative process known as maximal variation in order to obtain a variety of expertise

and perspectives.[254] We aimed to recruit 5 experts in order to have a good spread of expertise to

inform program development. A preliminary search through these sources identified 30 potential

experts (Table 3.5).

Table 3.5. Aim 1 Expert Recruitment Sources: A Preliminary Search to Gauge Feasibility

Source/Location	No. Experts Identified
American Pharmacists' Association (APhA) or American Association of Colleges of Pharmacy (AACP)	1
University	12
Community Pharmacy with Successful Naloxone Service	2
Department of Public Health	3
Clinical Practice or Substance Abuse Treatment Center	12
Total	**30**

Potential community pharmacist and expert participants were contacted by the primary

investigator (PI) via telephone, email, or fax with a maximum of 5 contact attempts. Study

eligibility was determined using a brief scripted inquiry, and interested parties were provided

with an information letter detailing the study via fax or email. The PI also obtained written

informed consent from eligible, interested parties via fax or email.

Stakeholder panel

Furthermore, based on their responses, level of enthusiasm, and willingness, a minimum

of two interviewed pharmacists and two interviewed experts were identified and contacted by

telephone or email during the recruitment process to serve as a "stakeholder panel" to provide feedback during the development of the naloxone training program. Participants were purposefully selected to represent a spread of independent/chain pharmacy and/or clinical/pedagogical perspectives using a maximal variation technique.[254]

Sample size calculation

Since the goal of this aim is to collect rich, qualitative data, a power calculation to determine sample size was not appropriate.[249] We estimated that saturation would be reached after 10 pharmacist interviews.[38,259] Assuming a 15% consent rate,[258] a sampling frame of 75 pharmacies was sufficient; the number of community pharmacies present in priority counties was adequate to meet this need (Table 3.3).

3.1.4 Measures and Data Collection:

Formative interviews

Qualitative, semi-structured telephone interviews were conducted to elicit pharmacists' current level of naloxone training, attitudes regarding naloxone dispensing in the community pharmacy, desired/needed training content and format, as well as individual, organizational and external barriers to dispensing naloxone in community pharmacies (Table 3.6). Current naloxone service implementation strategies were also explored. It was anticipated that interviews would last about 30 minutes. Interviews were conducted by the PI (LH), who has experience conducting qualitative interviews.[260] Prior to conducting interviews, the PI reviewed the interview protocol with a second independent researcher (GC) in order to confirm that questions were relevant and made sense (peer debriefing).[261] After the first one or two

interviews, investigators (LH and SW) reviewed the transcripts to make sure that all necessary follow-up questions were being used.[261] Interviews were audio-recorded and transcribed verbatim, and continued until the saturation point was reached after an anticipated 10 pharmacist interviews, and an anticipated maximal variety of 5 expert interviews.[38,259] The Rev.com transcription service was used to transcribe audio recordings; this service has been used by the investigators in the past.[40,262] After completion of interviews, participants each received one $20 gift card. Research shows that this guaranteed type of financial incentive is an effective means of promoting study participation.[263,264]

Table 3.6. Aim 1 Measures

Measure	Source	Variable Scale	Analysis
• **Demographics** **Age, gender, race, ethnicity, education, profession, pharmacy type, pharmacy size, daily prescription volume, years in practice, current naloxone dispensing status**	• Online, self-administered survey distributed to community pharmacists after conducting interviews	• Categorical multiple-choice questions	• Descriptive statistics
• **Attitudes** ○ **Perceptions of naloxone services** ○ **Perceptions of pharmacists' role in naloxone services** ○ **Perceptions of co-workers' views & norms** ○ **Perceptions of patients using naloxone services**	• Scripted, semi-structured telephone interviews w/ community pharmacists & opioid abuse experts	• Open-ended	• Open coding & thematic analysis using Atlas.ti software
• **Barriers and facilitators** ○ **Individual (training, confidence, knowledge, skills, values)** ○ **System/organizational (staffing, hours, funds, workflow, location)** ○ **External (reimbursement, climate, policies)**	• Open-ended questions informed by previous research[19,235,237-242] & investigators' clinical experience		
• **Training needs** ○ **Desired/needed content (billing, counseling talking points, naloxone product demonstration skills, identifying eligible patients, communication skills)** ○ **Desired format (online, paper, webinar, live CE, home-study CE)** ○ **Current level/extent of training**			

Interview protocol development and rationale

Scripted, semi-structured interview questions were open-ended and informed by the PI's clinical experience as well as barriers to pharmacy-based services adoption/implementation

identified by community pharmacists in previous research.[235,237-242] Preliminary, unpublished research from open observations and semi-structured interviews with community pharmacists in Alabama conducted as part of the PI's qualitative methods coursework indicated that pharmacists in Alabama viewed naloxone dispensing positively, despite a lack of education and training regarding dispensing of naloxone as an opioid abuse prevention strategy.[29] Furthermore, pharmacists described naloxone dispensing and opioid abuse prevention strategies as part of the normal workflow activities in a pharmacy, yet perceived barriers such as lack of knowledge about "rules and regulations" outweighed perceived facilitators like establishing systems to identify eligible patients.[29] Pharmacists also believed that opioid abuse was a problem in Alabama, although they perceived individuals other than pharmacists (physicians, patients, pharmaceutical companies, insurance companies) as the driving cause behind the problem.[29] These findings were used to help refine and guide the development of the semi-structured interview protocol (Appendix A).

A semi-structured interview protocol is well-suited to the topic under investigation, as little is known about Alabama community pharmacists' naloxone training needs (content and format), attitudes, and facilitators/barriers to naloxone service adoption/implementation. Compared to structured interviews, the semi-structured format allows for the use of more probing questions to elicit further meaning or clarify participants' responses; for example, the use of phrases such as "Tell me more about that" or "What do you think about that?" can be used to probe for deeper, richer information (Table 3.7).[249,254] Structured interviews typically use only a pre-specified set of questions and do not allow for this probing.[249,254] On the other hand, unstructured interviews usually use a topic guide and let the participant speak freely; while flexible, it may be difficult to keep participants on topic.[249,254]

Table 3.7. Advantages and Disadvantages of Structured, Semi-Structured, and Unstructured Interview Protocols[249,254]

	Structured	**Semi-structured**	**Unstructured**
Key Elements	• Often uses Likert scales or ranking questions • Closely follows the interview script	• Uses open-ended questions • Loosely follows the interview script	• Uses open-ended questions • Uses a topic guide only
Advantages	• Least time- and labor-intensive to analyze	• Can probe for deeper meaning & clarify responses • Can reveal unanticipated responses	• Can probe for deeper meaning & clarify responses • Most likely to reveal unanticipated responses
Disadvantages	• Less opportunity to probe for deeper meaning • Less likely to reveal unanticipated responses	• More time- and labor-intensive to analyze	• Most time- and labor-intensive to analyze • Difficult to keep participants on topic

Additionally, a telephone interview format was chosen to be most convenient for busy pharmacists and to decrease the need for travel to an in-person interview location (Table 3.8). Compared to in-person interviews, telephone interviews are less prone to social desirability bias.[249] In this case, a telephonic medium also presented an advantage over a self-administered questionnaire, as it allowed the interviewer to probe the participant for deeper meaning and clarification of response.[249,254]

Table 3.8. Advantages and Disadvantages of In-Person, Telephone, & Self-Administered Interview Protocols[249,254]

	In-person	Telephone	Self-administered Questionnaire
Advantages	• Can probe for deeper meaning & clarify responses • Can analyze participants' body language	• Less social desirability bias compared to in-person • Can probe for deeper meaning & clarify responses • Less expensive compared to in-person • Can interview participants over a wide geographic area	• Least social desirability bias • Can interview participants over a wide geographic area • Can easily ask rating/ranking questions
Disadvantages	• Most social desirability bias • Travel costs to interview location • Difficult to ask rating/ranking questions	• Cannot analyze participants' body language • Difficult to ask rating/ranking questions • Difficult to establish a rapport with the participants	• Difficult to probe for deeper meaning of clarify responses • Expense depends on distribution method (hardcopy vs online, etc)

Stakeholder panel: training program development and pre-testing

Needs and barriers elicited during these interviews informed the development of a

targeted naloxone training program. This program was created by the primary investigator, in

close consultation with the co-investigators and stakeholder panel. It was planned to consult the

stakeholder panel via telephone, videoconference, email, or in-person (depending on panelist

needs) 2-3 times to provide **feedback on the format and content** of the training program. This

participatory approach is shown to increase accessibility, usefulness, and end-users' motivation

to participate in training.[27,28] This also served as a pre-test of the program to confirm face and

content validity.[265] Feedback was recorded using an online questionnaire (Appendix B) and field

notes transcribed by the investigator, and findings were used to iteratively modify and finalize the training program. After completion of all feedback sessions, panelists each received a $50 financial incentive.

Training program pilot test

It was planned for the training program to be pilot tested by at least 5 community pharmacists in Alabama prior to implementation in Aim 2. However, due to time constraints and in order to remain within the study timeframe, the program was pilot-tested among 2 members of the PI's department (NH and TH). The pilot-test served as a soft-launch to further confirm usability and content validity of the training program, and feedback was used to finalize the training program.[266]

Potential training program elements

Depending on the results of interviews and stakeholder panel feedback, potential training formats included online, webinar, in-person, paper-based, or combination. Based upon the authors' previous research, paper-based or online live webinar was the anticipated preferred CE format,[29,30] and we expected 1 to 3 hours of CE credit to be offered.[40,228,267] Potential training topics also depended on interview and panel findings, but included: naloxone stocking and billing; patient counseling tips and talking points; product demonstration skills; strategies for approaching prescribers regarding naloxone prescriptions; strategies for identifying, approaching, and communicating with at-risk patients; strategies for co-prescribing of naloxone with chronic opioid prescriptions; and pharmacy-based naloxone services implementation checklists or guidelines.[31,32]

3.1.5 Data Analysis:

Descriptive statistics were used to analyze demographic data (Table 3.6). Interview

transcripts were analyzed by two independent researchers (the PI plus another investigator) with

Atlas.ti software (ATLAS.ti Scientific Software Development GmbH, Berlin, Germany) using

open coding and thematic analysis, with discrepancies resolved via discourse and consensus.[268]

Specifically, patterns within the data were first identified to generate open codes using in vivo,

value, and versus coding.[269] A second round of open coding was performed to reevaluate and

consolidate initial codes, followed by clustering of finalized codes into broad categories and

themes. To ensure trustworthiness and credibility of findings, peer debriefing was performed

after second level coding and after formation of initial themes; feedback from these sessions was

be used to refine final codes and themes.[254] Member checking was used to confirm the

trustworthiness of final themes.[254] Krippendorff's alpha was calculated as a measure of inter-

rater reliability. The investigators have used this method of qualitative data analysis successfully

in the past.[38,259]

3.2 <u>Specific Aim 2</u>: To evaluate a targeted naloxone training program among community
pharmacists in Alabama.

3.2.1 Hypotheses:

This aim sought to explore the effect of a targeted naloxone training program on Alabama

community pharmacists' knowledge, perceived barriers, attitudes, confidence, intention, and

number of naloxone prescriptions dispensed. We also assessed the individual technical and

social factors motivating participation in the naloxone training and adoption/implementation of pharmacy-based naloxone services, as well as organizational fulfillment of naloxone service structure and process indicators. Accordingly, our primary operating hypothesis was:

1. **Primary Hypothesis:** Receipt of a targeted naloxone training program will improve Alabama community pharmacists' perceived barriers, knowledge, attitudes, confidence, intentions, service structure and process implementation, and number of naloxone prescriptions dispensed.

Furthermore, we specifically hypothesized that:

1. H1a: Change in naloxone **knowledge** from baseline to post-training and baseline to 3-months will be greater among intervention compared to control group pharmacists.

2. H2a: Change in **intention** to dispense naloxone or perform naloxone services from baseline to post-training and baseline to 3-months will be greater among intervention compared to control group pharmacists.

3. H3a: Change in **attitudes** regarding naloxone services from baseline to post-training and baseline to 3-months will be greater among intervention compared to control group pharmacists.

4. H4a: Change in **confidence** regarding naloxone services from baseline to post-training and baseline to 3-months will be greater among intervention compared to control group pharmacists.

5. H5a: Change in rating of **perceived barriers** to naloxone services implementation from baseline to post-training and baseline to 3-months will be greater among intervention compared to control group pharmacists.

6. H6a: **Number of naloxone service structure activities completed** by the end of the 3-month study period will be greater among intervention compared to control group pharmacists.

7. H7a: **Number of naloxone service process activities engaged in** by the end of the 3-month study period will be greater among intervention compared to control group pharmacists.

8. H8a: Change in **number of naloxone prescriptions** dispensed from baseline to 3-months will be greater among intervention compared to control group pharmacists.

9. H9-11: **Knowledge, intention,** and **beliefs** (perceived barriers, attitudes, confidence) will be associated with performance of **behaviors** (number of structure activities completed (H9a), number of process activities engaged in (H10a), and number of naloxone prescriptions dispensed (H11a)) across 3 months.

A secondary, exploratory hypothesis examined pharmacists' motivations for participating in pharmacy-based naloxone services according to Kennedy and Fiss' Motivations for Adopting Innovation Model, which postulates that early adopters of an innovation are motivated by economic and social gains (versus losses), as well as opportunity framing (versus threat framing).[243] Therefore, we hypothesized that:

10. H12a: **Economic gains, social gains, and opportunity framing** will be associated with **intention** to dispense naloxone or perform naloxone services, as measured at baseline.

3.2.2 Research Design:

In order to test the hypotheses listed above, this aim was conducted using a pragmatic randomized controlled trial design with 3 time points at baseline (O1), post-training (O2), and 3 months (O3) (Figure 3.1).[270,271] This design was chosen in order to assess both immediate and sustained changes in pharmacists' knowledge, attitudes, confidence, and intention to dispense naloxone for opioid overdose death prevention after receipt of a targeted training program.

Figure 3.1. Research Design: Pragmatic Randomized Controlled Trial[270]

Intervention	O_1	X	O_2	O_3
Control	O_1		O_2	O_3
	Baseline		Post-Training	3 Months

Rationale for research design

This aim was conducted using quantitative methodology. Compared to qualitative methods, which was used in Aim 1 (3.1) as a formative step, the use of quantitative methods allowed us to assess the impact of the naloxone training program on our measures of interest (Table 3.1).[249,256] We were also able to assess quantifiable measures of naloxone service adoption and implementation. Additionally, this design allows us to generalize our potential findings to the larger population of community pharmacists in Alabama, whereas a qualitative methodology limits generalization.

Furthermore, the topic is well-suited to an experimental design (Table 3.9).[271,272] Compared to observational study designs, this design allows us to make causal, rather than just correlational, inferences. Depending on specific design elements, experimental studies may be more expensive or time- and labor-intensive compared to quasi-experimental studies. However,

experimental designs are advantageous in that they increase the ability to rule out threats to internal validity, such as history, maturation, and selection bias.[249] In regards to this particular topic of community pharmacy-based naloxone services adoption and implementation, there is a lack of two-group studies in the United States, and in Alabama in particular.[182] Therefore, a two-group pragmatic randomized controlled trial (RCT) was conducted in order to minimize threats to internal validity, while tailoring the recruitment and data collection strategies (3.2.3.) to maximize the feasibility of the study in terms of time, effort, and budget.[270]

Table 3.9. Advantages and Disadvantages of Observational, Quasi-Experimental, & Experimental Study Designs[249,271,272]

	Observational	Quasi-Experimental	Experimental
Key Elements	• Primary or secondary analysis • Cross-sectional, case-control, cohort designs	• Primary analysis • Does not use random assignment to create comparison groups • Pretest-posttest, time series designs • May or may not include a control group	• Primary analysis • Uses random assignment to create comparison groups • Explanatory or pragmatic RCT designs
Advantages	• Least expensive • Can use in cases where it is not feasible or ethical to use random assignment • Smaller sample size • Can explore multiple variables	• Can make causal inferences • Can use in cases where it is not feasible or ethical to use random assignment • More expensive • Smaller sample size • Less time- & labor-intensive recruitment • Easiest to rule out threats to external validity	• Can make causal inferences • Easiest to rule out threats to internal validity
Disadvantages	• Cannot make causal inferences	• Compared to experimental designs, more difficult to rule out threats to internal validity	• More expensive • Large sample size • Most time- & labor-intensive recruitment • Compared to quasi-experimental designs, more difficult to rule out threats to external validity

Pragmatic RCTs differ from traditional explanatory RCTs in several key ways: 1) they use less strict inclusion and exclusion criteria; 2) they focus on effectiveness rather than efficacy; 3) they focus on interventions or outcomes that are directly relevant to stakeholder needs; and 4) they take place in practice-based rather than well-controlled experimental settings (Table 3.10).[270,271] As a result, pragmatic trial designs offer improved external validity compared to traditional RCTs, and allow for a more time- and effort-friendly study while maintaining high levels of internal validity.[270,271] This is ideal for maintaining the feasibility and value of the current dissertation study.

Table 3.10. Key Elements of Explanatory vs Pragmatic Randomized Controlled Trials[270]

	Explanatory Trials	**Pragmatic Trials**
Similarities	• Uses random assignment to control & intervention groups	• Uses random assignment to control & intervention groups
Differences	• Focuses on efficacy • Well-controlled setting • Strict inclusion & exclusion criteria • Intervention / outcomes indirectly relevant to stakeholder needs • Maximizes internal validity	• Focuses on effectiveness • Practice-based setting • Less strict inclusion & exclusion criteria • Intervention / outcomes directly relevant to stakeholder needs • Maximizes external validity

3.2.3 Participants and Setting:

Inclusion and exclusion criteria

In order to generalize to our target population of community pharmacists in Alabama, community pharmacists throughout Alabama priority counties were our sample population (Table 3.3). The unit of analysis was at the individual pharmacist level. Individuals were eligible to participate if they were: a registered pharmacist; and employed full-time at a

community pharmacy located within a priority county in Alabama. Only one pharmacist per site was eligible to participate. Individuals who were employed at the same community pharmacy as another pharmacist enrolled in the study, or who participated as a stakeholder panelist in Aim 1, were excluded from participation. Pharmacists who participated in Aim 1 formative interviews were eligible for study participation, and pharmacists employed at a site that did not currently stock naloxone were allowed to participate in the study.

Sampling frame

Priority counties in Alabama were selected based on highest opioid death rate (3.1.3, Table 3.3). Community pharmacies were identified and contacted for recruitment from these priority counties using Hayes Directory. These pharmacies included those recruited in Aim 1, but also expanded the sampling frame to target all priority counties simultaneously. Only one pharmacist per location was eligible to participate.

Sample size calculation

The most conservative values providing sample size estimates that could be feasibly recruited given the time and funding constraints of this dissertation study while providing adequate power were chosen. Based on an effect size of 23% (expected increase in knowledge score after the training) and standard deviation of 26%,[273,274] a minimum total sample size of 44 (22 per group) was predicted to be sufficient to evaluate our measures of interest with 80% power.[275] Assuming a 20% drop-out rate,[276,277] a total sample size of 54 (27 per group) was required for the study to be powered to detect differences between groups. Supposing a consent rate of 15%,[258] a sampling frame of 240 pharmacies was sufficient to reach our desired sample

size; the number of community pharmacies present in priority counties was more than adequate

to meet this need (Table 3.3). Therefore, community pharmacies from amongst priority counties

in Alabama served as the final sampling frame for recruitment.

Table 3.11. Sample Size Estimation[273,274]

	Before Attrition	Attrition 10%	Attrition 15%	Attrition 20%
Effect Size +/- Std[a]	**Sample Size (N)**			
22 +/- 18%	24, 12/group	26, 13/group	28, 14/group	30, 15/group
22 +/- 37%	92, 46/group	102, 51/group	106, 53/group	110, 55/group
23 +/- 26%	44, 22/group	48, 24/group	50, 25/group	**54, 27/group**
25 +/- 23%	30, 15/group	32, 16/group	34, 17/group	36, 18/group

[a]Change in knowledge score after training

Recruitment and procedures

Pharmacists in priority counties were recruited to participate in the training program via

email, fax, phone and postal mail using multiple contacts (Figure 3.2).[278] Specifically, a mailed

recruitment postcard was used to advertise the study and how to enroll, along with an email sent

to all pharmacists registered with the Alabama Board of Pharmacy. Email addresses were

obtained through the Office of Postgraduate Education at the PI's institution. Pharmacists were

directed to visit the study website at www.EmpoweringCommunityPharmacists.org, where they

could view an information letter more fully describing the study, as well as indicate their interest

in participating in the study via an online interest form, which included eligibility screening

questions. If no response was obtained after one week, a reminder fax, email, or telephone call

was sent, followed by a replacement postcard if there was no response after 1 more week, and a

final reminder fax, email and/or telephone call if there was still no response after 1 more week.

After individuals indicated their interest in enrolling, the PI called them to answer any questions

and explain the consent process. Written informed consent was obtained from interested parties

via fax or email. This method of recruitment has been used in previous studies to enroll

community pharmacists in Alabama with a high response rate.[278,279]

Figure 3.2. Aim 2 Recruitment Strategy

Initial postcard mailing & email	Reminder fax, email or telephone call	Replacement postcard	Reminder fax, email or telephone call	Randomize to control or intervention
1 week	*1 week*	*1 week*	*1 week*	

Depending on rate of recruitment, two-month rolling enrollment into the naloxone

training program was planned (section 3.3). If sub-optimal enrollment rates were encountered,

we planned to supplement the recruitment strategies outlined above with purposive telephone,

fax, and/or email contacts throughout priority counties over the 2-month enrollment window. To

incentivize recruitment, participants received continuing education (CE) credit after completing

the training, as well as one $10 financial incentive after completing the O1 and O2 surveys, and a

second $15 after completing the 3-month (O3) survey.

Steps to limit contamination

Due to the two-group design of this aim, contamination (spread of training materials from

intervention to control group pharmacists) was a vital concern that could threaten the internal

validity of the study. In order to minimize the opportunity for contamination, only one

pharmacist from each pharmacy location was eligible to participate in the study. This element

was closely screened via the interest form prior to consent and randomization. If multiple

pharmacists from the same pharmacy sign up via the interest form, the PI contacted them by

email or telephone to explain that only one pharmacist could participate in the study; however,

after the study was complete, we would release the information from the naloxone training program.

Group allocation and blinding

After informed consent was obtained, pharmacists were randomized to a control or intervention group using a computerized random number generator. Group allocation was 1:1, stratified based on pharmacy type (chain or independent). Due to the nature of the data collection process, it was not possible for the PI or participants to be blinded to group membership or to the outcomes being assessed.

3.2.4 Intervention

The targeted naloxone training program developed in Aim 1 (3.1.4) was delivered to intervention group pharmacists after completion of the baseline survey (Table 3.12, Figure 3.3). Control group pharmacists did not receive the targeted training, but only received general information about naloxone (eligible patients, dosage forms, how to administer) in the form of a pre-existing publicly available flyer available from the PrescribetoPrevent.org[195,280] (Appendix C); the same flyer was provided to intervention participants at the time of the training. This ensured that all participants had access to basic technical information about naloxone for patient care. In order to promote participant retention in the study, all participants were also contacted by email at one and two months post-training. These emails or interim contacts served as a reminder of study enrollment and participants were provided with: 1) recently published articles on opioid-related topics (control and intervention groups);[281-284] and 2) resources to aid naloxone services implementation, including Alabama naloxone standing order, prescriber fax

communication form, risk assessment form publicly available from Operation Naloxone, patient

education flyer, and waiting room flyer (intervention group only) (Appendix D.1-D.5).

Although the effectiveness of the training program was not assessed among control group

pharmacists, they were offered the training program after completion of the dissertation study as

a benefit of their participation. The training program, which aims to increase pharmacists'

knowledge and ability to dispense naloxone and promote adoption/implementation of pharmacy-

based naloxone services, was provided to participants free of charge. Upon completion of the

program, pharmacists received continuing education (CE) credit. The exact length of the

program and associated CE credit were dependent on information gained from formative

interviews and the stakeholder panel in Aim 1 (3.1.4) and are presented in the Results section;

however, based on our experiences creating previous training programs, we expected 1 to 3

hours of CE credit to be offered.[40,228,267]

Table 3.12. Aim 2 Intervention Strategies

Intervention	Implementation Strategy/Target	Time
Naloxone training program (CE)	Education	Between O1 and O2
Flyer	Technical competency	Between O1 and O2
Interim email contact	Reminder/nudge	1 & 2 months post-training

Figure 3.3. Aim 2 Procedures and Intervention
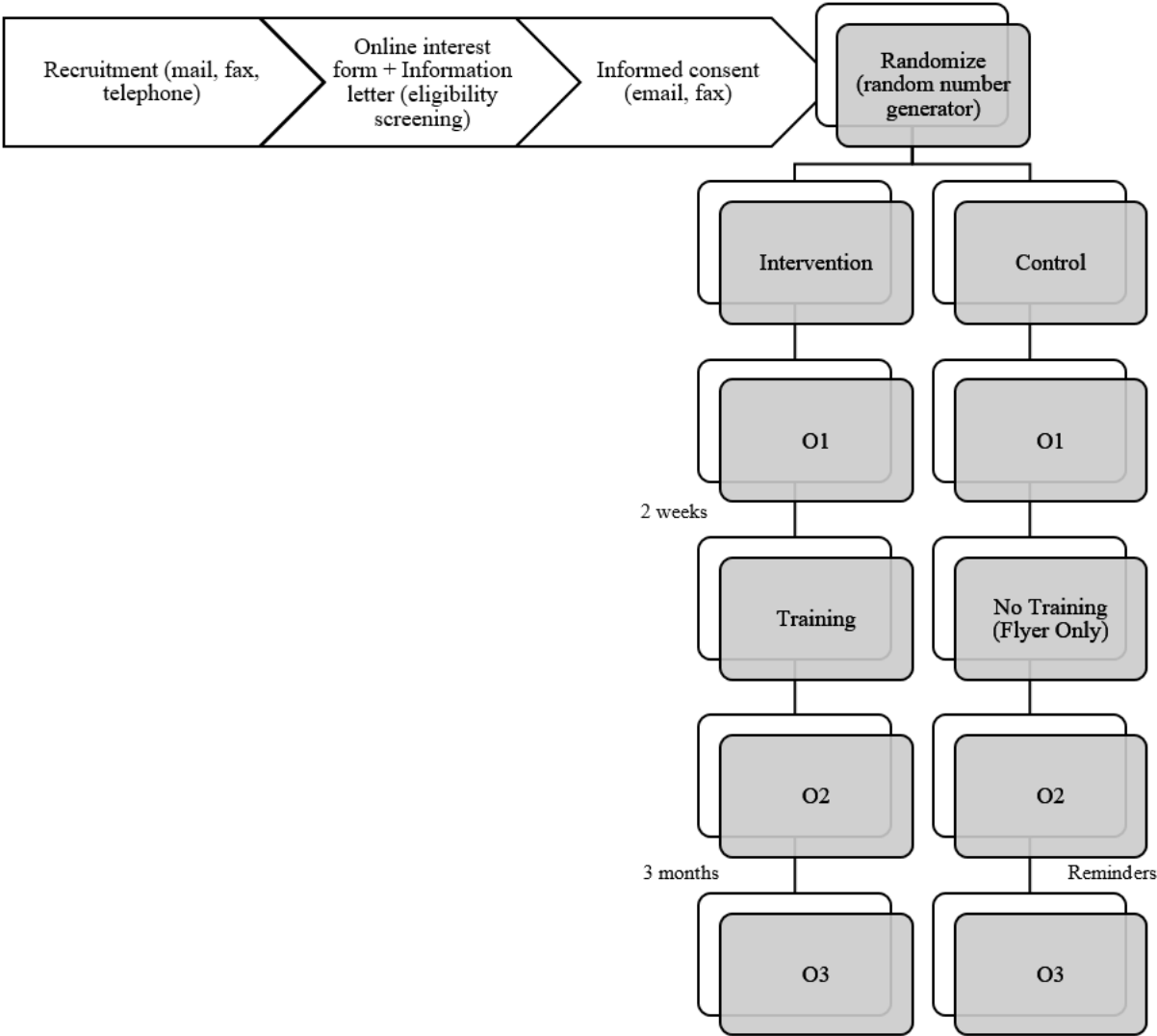
3.2.5 Measures and Data Collection:

Data was collected from intervention and control group participants using an online survey distributed via email at baseline (2 weeks prior to beginning the training, O1), immediately post-training (with a 1-month completion window, O2), and 3 months post-training (with a 1-month completion window, O3). Online surveys were expected to take 15-20 minutes to complete. The online survey instrument was newly constructed based on previous research[11,19-21,243] and the investigators' clinical knowledge, and was **pre-tested** among members of the PI's department to ensure face and content validity as well as adequate scale spread. **Primary outcome measures** were collected at O1, O2, and O3 and included: knowledge about naloxone; perceived barriers to adoption/implementation of pharmacy-based naloxone services; attitudes regarding pharmacy-based naloxone services; confidence in performing naloxone dispensing behaviors; and intention to dispense naloxone or perform naloxone services (Table 3.13). The **secondary outcome measures**, including self-reported naloxone dispensing behaviors (encompassing fulfillment of naloxone services structure and process indicators) and number of naloxone prescriptions dispensed in the past 3 months, were collected at O1 & O3. Change in naloxone dispensing behaviors and number of naloxone prescriptions dispensed were not assessed at O2 because the intervention's impact on beliefs was expected to be more immediate compared to the impact on behaviors. Factors motivating pharmacists' adoption/implementation of naloxone services and/or participation in the naloxone training program according to Kennedy and Fiss' (2009) Motivations for Adopting Innovation Model[243] were also assessed at O1.

This study gathered data to first verify the effect of the training on pharmacists' knowledge, perceived barriers, attitudes, confidence, intention, and naloxone dispensing

behaviors. This will serve as a preliminary confirmation of the conceptual model (Figure 2.3) before more rigorous evaluation of dispensing practices or patient outcomes is performed. <u>If an increase in pharmacists' knowledge, attitudes, confidence, and intention is demonstrated in the study, future studies will use more objective measures to evaluate naloxone dispensing behaviors over a greater time period. Furthermore, future studies may use claims data as a more objective assessment of number of naloxone prescriptions dispensed.</u>

Instrument development and rationale

The constructs in our survey instrument can be lumped into 5 broad categories or domains: 1) knowledge; 2) intention; 3) beliefs; 4) behaviors; and 5) motivation factors (see Appendix E for full survey).

Knowledge category

First, regarding the knowledge category, 7 questions were constructed by the investigators in a multiple-choice format (Table 3.13). Topics were informed by current knowledge-based naloxone training programs, current substance abuse literature, and information from the authors' unpublished work[29,117] as well as clinical knowledge. Questions were also adapted from an existing knowledge measure by Nielsen et al[182] and the Opioid Overdose Knowledge Scale (OOKS) developed by Williams et al (Cronbach's alpha = 0.83).[285]

Intention category

Second, intention to dispense naloxone or perform naloxone services was measured. Five items were measured using a 7-point Likert-type scale from 1=strongly disagree to 7=strongly agree. A 7-point Likert-type scale was chosen as opposed to a 5-point scale based on research

recommending the use of as large a range as practicable, with 7-point scales being the highest

reliable range, which may then be collapsed down into fewer categories if needed.[286]

Furthermore, Spencer et al showed that aggregated Likert scale items and individual Likert items

using at least 5 item response options may be analyzed as continuous rather than ordinal data,

which streamlines the analysis.[287] We also chose to use an odd number of response options (as

opposed to an even number) and retain the "neutral" position to avoid a forced response.[286]

Items measuring intention were created by the investigators and informed by the Theory of

Planned Behavior,[248] and adapted from an existing measure by Urmie et al, who measured

intention to provide MTM services in a population of pharmacy students in Iowa (Cronbach's

alpha = 0.84).[288]

Beliefs category

Third, the beliefs category included 3 constructs: perceived barriers to pharmacy-based

naloxone services adoption/implementation; attitudes regarding pharmacy-based naloxone

services; and confidence to perform naloxone services.

Survey items for barriers (20 items), attitudes (15 items), and confidence (10 items) were

developed by the investigators and informed by MTM services literature,[46,186,233-236] the limited

naloxone services literature available,[11,19-21,173,182,289] and the authors' previous research.[29,117]

Survey items were also adapted from existing measures by Nielsen et al, who measured barriers,

attitudes, and confidence in a population of Australian community pharmacists (Cronbach's

alpha for attitudes construct = 0.797; internal consistency was not reported for other

constructs).[182] Barriers were further informed by the Consolidated Framework for

Implementation Research (CFIR).[245]

Behaviors category

Fourth, the behaviors category included 3 constructs: naloxone service structure indicators; process indicators; and number of naloxone prescriptions dispensed in the past 3 months. Structure indicators (16 items) were measured using a 7-point Likert-type scale from 1=no progress to 7=completed, and process indicators (16 items) were measured on a 7-point Likert-type scale from 1=never to 7=extremely frequent. Structure and process indicator items were created by the investigators and informed by the Consolidated Framework for Implementation Research (CFIR),[245] with survey items adapted from an existing measure previously developed by the authors.[290] Number of naloxone prescriptions dispensed in the past 3 months was measured via self-report. Although self-reported measures may be subject to recall and social desirability bias, more objective measures like obtaining dispensing logs from pharmacies are burdensome for busy pharmacists and likely to decrease survey response rates.[40] Furthermore, this study will serve as a proof-of-concept prior to conducting future studies using more objective measures of dispensing like pharmacy claims data.

Motivation factor category

Lastly, factors motivating naloxone services adoption/implementation were also measured. Motivation factor constructs included economic gains and losses, social gains and losses, opportunity and threat framing, as well as technical efficacy and social legitimacy. Seventeen items were measured using a 7-point Likert-type scale from 1=strongly disagree to 7=strongly agree. This construct was informed by Kennedy and Fiss' Motivations for Adopting Innovation Model.[243] Survey items were also adapted from the authors' previous research.[267]

Table 3.13. Aim 2 Measures

Measure	Source (Time)	Scale	Analysis
• **Demographics** Age, gender, race, ethnicity, education, job title, pharmacy type, daily prescription volume, years in practice, FTEs employed, frequency of opioid Rxs	• Online survey (O1) • Multiple-choice questions	• Categorical	• Descriptive statistics
KNOWLEDGE (Primary)			

• **Knowledge**
  o **General opioid knowledge**
  o **Naloxone patient counseling**
  o **Naloxone mechanism of action**
  o **Naloxone state laws**
  o **Naloxone products, billing and stocking**
	• Online survey (O1, O2, O3)
	• Multiple-choice questions (percent correct)
	• Informed by previous research[117] & adapted from Nielsen et al.[182] and the OOKS[285]
	• Example question: *"What is the onset of action for naloxone?"*
		• Continuous
		• 7 items
			• Descriptive statistics
			• Knowledge score will be calculated as percent correct
			• Mixed ANOVA ($\alpha=0.05$)
			• Bonferroni post-hoc tests
			• KR-20 for internal consistency

INTENTION (Primary)			

• **Intention to dispense naloxone or perform naloxone services in the next 3 months (Primary)**
  o **Identifying eligible patients**
  o **Dispensing naloxone**
  o **Communicating with providers regarding naloxone**
	• Online survey (O1, O2, O3)
	• 7-point Likert-type scale from 1=strongly disagree to 7=strongly agree
	• Informed by the Theory of Planned Behavior[248] & adapted from Urmie et al[288]
	• Example question: *"In the next 3 months, I plan to stock naloxone in my pharmacy"*
		• Ordinal
		• 5 items
			• Descriptive statistics
			• Scores will be summed to create total scale scores
			• Mixed ANOVA ($\alpha=0.05$)
			• Bonferroni post-hoc tests
			• Cronbach's alpha for internal consistency
			• Exploratory factor analysis for construct validity

BELIEFS (Primary)			

• **Barriers to adopting/implementing (Primary)**
  o **Management support**
  o **Staffing, funds, workflow, location**
  o **Technical support**
  o **Organizational culture**
  o **Individual attitudes, values**
  o **Factual knowledge, training, skills**
	• Online survey (O1, O2, O3)
	• 7-point Likert-type scale from 1=strongly disagree to 7=strongly agree
	• Adapted from Nielsen et al.[182] & informed by the Consolidated Framework for Implementation Research (CFIR)[245]
	• Example question: *"It is too time-consuming to provide naloxone services"*
		• Ordinal
		• 20 items
			• Descriptive statistics
			• Scores will be summed to create total scale scores
			• Mixed ANOVA ($\alpha=0.05$)
			• Bonferroni post-hoc tests
			• Cronbach's alpha for internal consistency
			• Exploratory factor analysis for construct validity

• **Attitudes (Primary)**
  o **Perceptions of naloxone services**
  o **Perceptions of pharmacists' role in naloxone services**
  o **Perceptions of co-workers' views & norms**
  o **Perceptions of patients using naloxone services (stigma)**
	• Online survey (O1, O2, O3)
	• 7-point Likert-type scale from 1=strongly disagree to 7=strongly agree
	• Adapted from Nielsen et al.[182]
	• Example question: *"I believe that supplying naloxone will encourage people to abuse opioids more"*
		• Ordinal
		• 15 items	

• **Confidence (Primary)**
  o **Identifying eligible patients**
  o **Dispensing naloxone**
  o **Communicating with providers regarding naloxone**
  o **Billing and stocking naloxone**
	• Online survey (O1, O2, O3)
	• 7-point Likert-type scale from 1=strongly disagree to 7=strongly agree
	• Adapted from Nielsen et al.[182]
	• Example question: *"I am confident in my ability to proactively identify patients who would benefit from naloxone"*
		• Ordinal
		• 10 items	

BEHAVIORS (Secondary)			

• **Structure activity completion in the past 3 months**
  o **Establishing staff member roles**
  o **Gaining management support**
  o **Setting a goal for naloxone services**
  o **Ensuring workflow is appropriate**
  o **Ensuring staffing is adequate**
  o **Billing & stocking procedures in place**
  o **Business plan in place**
  o **Ensuring access to resources or support**
  o **Ensuring technical support**
	• Online survey (O1, O3)
	• 7-point Likert-type scale from 1=no progress to 7=completed
	• Number of activities completed
	• Informed by the Consolidated Framework for Implementation Research (CFIR)[245] and previous research[290]
	• Example question: *"Over the past 3 months, I created a business plan for naloxone services at my pharmacy"*
		• Ordinal
		• 16 items
			• Descriptive statistics
			• Scores will be summed to create total scale scores
			• Mixed ANOVA (α=0.05) for scores
			• Generalized estimating equations (GEE) with log-link function to explore relationship of number of activities completed/engaged in with knowledge, intention, & beliefs

• **Process activity engagement in the past 3 months**
  o **Stocking naloxone**
  o **Performing chart review (or other method) to identify at-risk/eligible patients**
  o **Encountering a potentially eligible patient**
  o **Counseling potentially eligible patients**
  o **Recommending naloxone to eligible patients**
  o **Contacting the prescriber regarding naloxone for a patient**
  o **Dispensing naloxone to an eligible patient**
	• Online survey (O1, O3)
	• 7-point Likert-type scale from 1=never to 7=very frequently
	• Number of activities engaged in
	• Informed by the Consolidated Framework for Implementation Research (CFIR)[245] and previous research[290]
	• Example question: *"Over the past 3 months, I proactively identified at-risk patients who would benefit from naloxone"*		

• **Number of naloxone prescriptions dispensed in the past 3 months**	• Online survey (O1, O3) • Self-report (queried from pharmacy dispensing system)	• Continuous	• Mann-Whitney U & Wilcoxon Signed Rank (α=0.05) • GEE with log-link function to explore relationship of number of prescriptions dispensed with knowledge, intention, & beliefs
MOTIVATION FACTORS (Secondary)			

• **Factors motivating naloxone services adoption / implementation**
  o **Economic gains vs economic losses**
  o **Social gains vs social losses**
  o **Opportunity framing vs threat framing**
  o **Technical efficacy vs social legitimacy**
	• Online survey (O1)
	• 7-point Likert-type scale from 1=strongly disagree to 7=strongly agree
	• Informed by Kennedy & Fiss' (2009) Motivations for Adopting Innovation Model[243] and previous research[267]
	• Example question: *"If I implement naloxone services, it will increase my pharmacy's image in the community"*
		• Ordinal
		• 17 items
			• Descriptive statistics
			• Scores will be summed to create total scale scores
			• Multiple linear regression to explore relationship with intention
			• Cronbach's alpha for internal consistency

3.2.6 Data Analysis:

Descriptive statistics were used to analyze demographic data (Table 3.13). Knowledge,

intention, belief, and behavior constructs were also characterized using descriptive statistics.

Intention, belief, behavior, and motivation factor scale items were reverse coded if necessary.

All analyses were performed using IBM SPPS Statistical Software version 24 (IBM, Armonk,

NY) or SAS software version 9.4 (SAS Institute Inc., Cary, NC) with an a priori alpha level of

0.05. Detailed descriptions of analyses for constructs are presented in the following sections.

Knowledge

Knowledge scores were calculated based on the percent of questions correct (Table 3.13).

Change in mean knowledge scores at O1, O2, and O3 was compared between control and

intervention pharmacies using two-way mixed ANOVA with Bonferroni post-hoc tests.[291] Two-

way mixed ANOVA is similar to the two-way repeated measures ANOVA, but can be used in

cases where there are both "within subjects" and "between subjects" factors (Table 3.14).[291] In

this case, time (O1, O2, or O3) serves as the "within-subjects" factor, and group (intervention or

control) serves as the "between-subjects" factor.

Table 3.14. Similarities and Differences Between Common Two-Way ANOVA Tests[291]

	Two-Way Between-Subjects ANOVA	Two-Way Repeated Measures ANOVA	Two-Way Mixed ANOVA
Similarities	• Used to assess if there is an interaction effect between 2 independent variables on a dependent variable	• Used to assess if there is an interaction effect between 2 independent variables on a dependent variable • Independent variables measured over time	• Used to assess if there is an interaction effect between 2 independent variables on a dependent variable • Independent variables measured over time
Differences	• Independent variables not measured over time	• All subjects receive all treatments / conditions	• Subjects receive only one treatment / condition
Within-Subjects Factor		✓✓	✓
Between-Subjects Factor	✓✓		✓

Intention and Beliefs

Scores on intention, barrier, attitude, and confidence scales were summed, and change in mean scale scores at measured time-points was compared between control and intervention groups using two-way mixed ANOVA with Bonferroni post-hoc tests.

Behaviors

Structure and process indicators

Extent of pharmacy-based naloxone service structure and process implementation was assessed in two ways. First, mean number of structure activities completed (response option=7) and mean number of process activities engaged in (response options=2-7) over 3 months was compared between control and intervention groups using tow-sided Mann Whitney U tests. The number of pharmacies that completed/engaged in each activity indicator over the study period, as well as the number that implemented structure or process activities fully (all activities completed/engaged in) or partially (not all activities completed/engaged in) were also compared between intervention and control using Fisher's Exact test. This allowed us to examine the level of overall completion/engagement in naloxone services implementation.

Second, scores on structure and process scales were summed, and change in mean item and scale scores at O1 and O3 were compared between control and intervention groups using two-way mixed ANOVA. This allowed us to examine the progress made in naloxone service structure and process activity fulfillment from baseline to 3 months in finer detail.

Number of naloxone prescriptions dispensed

The change in number of naloxone prescriptions dispensed at O1 and O3 was compared within and between control and intervention pharmacies using Wilcoxon Signed Rank test for matched pairs and Mann Whitney U test, respectively.

Motivation factors

Scores on economic gains, economic losses, social gains, social losses, opportunity framing, threat framing, technical efficacy, and social legitimacy scales at O1 were summed to create 8 total scale scores. Mean scale scores were compared within participants using paired-sample t-tests to find the most motivating factors.

Multiple linear regression was used to explore the relationship between motivation factors (as represented by scale scores) and intention to perform pharmacy-based naloxone services at baseline. Simple models may look like this:

$Y_{intention}$ = economic_gains + economic_losses + social_gains + social_losses

$Y_{intention}$ = technical_efficacy + social_legitimacy

$Y_{intention}$ = opportunity_framing + threat_framing

Association between knowledge, intention, beliefs, and behaviors

Generalized estimating equation (GEE) models for a negative binominal distribution with log-link function were also be used to explore the relationship between knowledge, intention, and beliefs (perceived barriers, attitudes, confidence) with number of naloxone prescriptions dispensed and number of service structure/process activities completed/engaged in. Within these models, we also controlled for the effect of confounders such as pharmacist gender, pharmacy type (independent versus chain), pharmacy location (urban versus rural), and average

daily prescription volume on number of naloxone prescriptions dispensed and extent of service

structure and process implementation. For example, a simple model may look something like:

$$Y_{naloxone\_rx} = knowledge\_score + perceived\_barriers + attitudes + confidence + intention +$$

$$person + group + time + time*group + gender + pharmacy\_type + location + rx\_volume$$

Reliability and validity

Internal consistency of the scales was measured using KR-20 (knowledge) and

Cronbach's alpha (barriers, attitudes, confidence, intentions, motivation factors). Exploratory

factor analysis was used to confirm construct validity for scales in the belief and motivation

factor domains.

Plan for dealing with missing data

In order to minimize missing data from item non-response, the online surveys were

constructed using "forced response" options, such that participants were required to complete all

survey items before moving on to the next section of the survey. There was missing data at some

time points due to item or survey non-response. In cases of item non-response, the respondent

was still included in analyses across time points for non-missing items. In cases of survey non-

response, the respondent was not included in analyses across time points.

3.3 Timeline

Activity	Month											
	1	2	3	4	5	6	7	8	9	10	11	12
Aim 1 – Recruitment	x	x										
Aim 1 – Interviews & data analysis	x	x	x									
Aim 1 – Develop & finalize training program	x	x	x	x	x							
Aim 2 – Recruitment					x	x						
Aim 2 – Training program roll-out						x	x					
Aim 2 – Collecting outcomes (O1, O2, O3)						x	x	x	x	x		
Aim 2 – Analysis							x	x	x	x	x	
Presentations, manuscripts, defense, final report									x	x	x	x

Chapter 4. Results

Results are presented separately for Aims 1 and 2. For Aim 1, findings from qualitative interviews are reported, including pharmacist and expert interviews. This is followed by results from multiple rounds of stakeholder panel feedback and details about the final format and content of the naloxone training program that was developed. Regarding Aim 2, results from the 3-month pragmatic randomized controlled trial are reported, including change in knowledge about naloxone, intention to provide naloxone services, beliefs about naloxone services (confidence, attitudes, and perceived barriers), behaviors (naloxone service structure activities completed, process activities engaged in, and number of naloxone prescriptions dispensed), and factors motivating participation in naloxone services. Finally, associations between the preceding outcome measures are explored.

4.1 Specific Aim 1: To incorporate community pharmacists' training needs and experts' strategies to overcome barriers regarding pharmacy-based naloxone services implementation into the development of a targeted training program in Alabama.

4.1.1 Participant Characteristics

A total of 16 interviewees were recruited (n=10 pharmacists, n=6 experts). Pharmacist and expert characteristics are presented below.

Pharmacists

A total of 10 community pharmacists were interviewed (Table 4.1a and 4.1b). Saturation was approached at 8 interviews, and 2 additional interviews were conducted to confirm that no

new information was gained, with saturation thus being reached after 10 interviews. The majority of pharmacists were female (70.0%), white (80.0%), and held a doctoral-level clinical pharmacy (PharmD) degree (90.0%). Only one interview participant had post-doctoral (residency) training.

The majority of participants' community pharmacies were independently-owned (80.0%) and located in urban counties in Alabama (80.0%). Seventy percent of interviewees' pharmacies dispensed opioid prescriptions more than 10 times daily, and while 70% kept some form of naloxone in stock, a mean (SD) of only 6.86 (6.49) naloxone prescriptions were reported being dispensed in the past 12 months.

Table 4.1a. Pharmacist Characteristics (N=10) [a]

Pharmacists (N=10)	
Characteristics	**n (%)**
Sex	
Male	3 (30.0)
Female	7 (70.0)
Race	
White/Caucasian	8 (80.0)
Black/African American	1 (10.0)
Asian or Pacific Islander	1 (10.0)
Ethnicity	
Hispanic	0
Non-Hispanic	10 (100.00)
Level of Education [b]	
BSPharm	2 (20.0)
PharmD	9 (90.0)
Masters degree	0
PhD	0
Residency	1 (10.0)
Fellowship	0
Job Title	
Staff pharmacist	2 (20.0)
Pharmacist-in-charge or pharmacy manager	4 (40.0)
Pharmacist owner/partner	4 (40.0)
Type of Pharmacy	
Corporately-owned	2 (20.0)
Independently-owned	8 (80.0)
Pharmacy Location by Alabama County	
Jefferson County, AL	2 (20.0)
Walker County, AL	1 (10.0)
Blount County, AL	1 (10.0)
Mobile County, AL	4 (40.0)
Madison County, AL	1 (10.0)
Pharmacy Location by Rurality [c]	
Urban	8 (80.0)
Rural	2 (20.0)
Frequency of Dispensing Opioid Prescriptions	
Less than 5 times daily	2 (20.0)
5-10 times daily	1 (10.0)
More than 10 times daily	7 (70.0)
Naloxone Kept in Stock	
Yes	7 (70.0)
No	3 (30.0)
Characteristics	**Mean (SD)**
Age, years	41.00 (9.31)
Number of years practicing pharmacy	14.90 (10.41)
Number of years at current pharmacy site	8.05 (5.42)
Number of naloxone prescriptions dispensed in the past 12 months	6.86 (6.49) [range: 1-20]

[a] Demographic information was collected via online survey post-interview.

[b] Participants were instructed to select all that applied.

[c] Rurality determined via zip codes using RUCA3.0 codes where 1-6=urban and 7-10=rural.

Themes and representative quotes identified from pharmacist interviews are presented in a later section (Section 4.1.2). In order to put representative quotes into context, each interviewee was assigned a unique codename and their characteristics are presented below (Table 4.1b).

Table 4.1b Pharmacist Characteristics by Individual Codename (N=10)

Codename	Age (Years)	Sex	Race	Job Title	Pharmacy Type	Pharmacy Location
P1	45	Male	White	Owner / partner	Independently-owned	Urban
P2	55	Female	Black	Staff pharmacist	Corporately-owned	Urban
P3	46	Female	White	Owner / partner	Independently-owned	Urban
P4	30	Female	White	Pharmacist-in-charge	Independently-owned	Urban
P5	56	Female	White	Owner / partner	Independently-owned	Rural
P6	37	Male	White	Pharmacist-in-charge	Corporately-owned	Urban
P7	32	Female	White	Pharmacist-in-charge	Independently-owned	Rural
P8	33	Female	White	Staff pharmacist	Independently-owned	Urban
P9	41	Female	White	Owner / partner	Independently-owned	Urban
P10	35	Male	Asian	Pharmacist-in-charge	Independently-owned	Urban

Experts

A total of 6 experts were interviewed (Table 4.2a and 4.2b). Similar to the community pharmacist interviews, a majority of expert participants were female (66.7%) and white (83.3%). In contrast to the community pharmacist participants, a greater number of experts had post-doctoral training (20.0% BSPharm, 40.0% Master's degree, 80.0% residency, 60.0% fellowship). Furthermore, experts came from a variety of practice sites, including academia (100.0%),

ambulatory care (33.3%), hospital acute care (33.3%), and public health department (33.3%).

Expert practice sites were located throughout the U.S., including Alabama (33.3%), Texas

(16.7%), New Mexico (16.7%), Rhode Island (16.7%), and Oregon (16.7%).

Table 4.2a Expert Characteristics (N=6) [a]

Experts (N=6)	
Characteristics	**n (%) [c]**
Sex	
Male	2 (33.3)
Female	4 (66.7)
Race	
White/Caucasian	5 (83.3)
Black/African American	0
Asian or Pacific Islander	1 (16.7)
Ethnicity	
Hispanic	0
Non-Hispanic	5 (100.0)
Level of Education [b]	
BSPharm	1 (20.0)
PharmD	5 (100.0)
Masters degree	2 (40.0)
PhD degree	0
Residency	4 (80.0)
Fellowship	3 (60.0)
Main Practice Site(s) [b]	
Academia	6 (100.0)
Ambulatory Care	2 (33.3)
Hospital	2 (33.3)
Public Health	2 (33.3)
Main Practice Site Location (State)	
Alabama	2 (33.3)
Texas	1 (16.7)
New Mexico	1 (16.7)
Rhode Island	1 (16.7)
Oregon	1 (16.7)
Characteristics	**Mean (SD)**
Age, years	37.00 (6.44)
Number of years at current practice site	6.00 (2.58)

[a] Demographic information was collected via online survey post-interview.
[b] Participants were instructed to select all that applied.
[c] Percentages may differ due to survey non-response.

Themes and representative quotes identified from expert interviews are presented in a later section (Section 4.1.3). In order to put representative quotes into context, each interviewee was assigned a unique codename and their characteristics are presented below (Table 4.2b).

Table 4.2b Expert Characteristics by Individual Codename (N=6)

Codename	Age (Years)	Sex	Race	Main Practice Site(s)	Practice Location
E1	NR	Female	White	Hospital or Acute Care	Alabama
E2	34	Female	White	Hospital or Acute Care	Alabama
E3	35	Female	White	Ambulatory Care	Oregon
E4	45	Female	Asian	Academia	New Mexico
E5	29	Male	White	Academia Ambulatory Care Public Health	Texas
E6	42	Male	White	Academia Public Health	Rhode Island

NR = no response.

4.1.2 Pharmacist Interviews

Pharmacist interviews averaged 36.37 minutes in length with 363.65 minutes (6.06 hours) recorded overall for all pharmacist interviews. An average of 5,118 words were transcribed per interview, for a total of 51,182 words overall.

As thematic analysis was conducted using a process of inductive open-coding, multiple rounds of coding were required to refine initial codes and generate final codes and themes. As pharmacists discussed multiple topic areas during interviews, final themes were also grouped into broad categories for ease of presentation. In order to clarify how results are presented in future sections, an overview of the elements used in thematic analysis is presented in Table 4.3.

107

Table 4.3 Definitions of Elements Used in Thematic Analysis

Thematic Analysis Elements	Definition
Code	Classifications applied to "units of meaning" within the interview transcript
Theme	Larger meaning derived from groups of codes
Category	Broad topic areas comprised of several themes

Overall, four rounds of coding were conducted to compile finalized codes, themes, and categories (Table 4.4, Figure 4.1). These rounds were iterative processes of review, discourse, and consensus with a second independent investigator (Kavon Diggs, KD). Round 1 generated initial codes (216 codes), which were refined in Round 2 (179 codes). Round 3 generated finalized codes by combining similar codes or excluding irrelevant codes, as well as initial themes and categories in consensus with a second investigator (137 codes, 46 themes, 11 categories). Themes and categories were finalized in Round 4 (137 codes, 53 themes, 11 categories) by refining theme and category names, as well as combining similar themes and splitting too broad of concepts into multiple more specific themes.

Table 4.4 Actions Taken Across Four Rounds of Coding Pharmacist Interview Transcripts

Coding Round	Actions / Purpose	Investigators (n)
1	Generated initial codes	1
2	Refined initial codes	1
3	Finalized codes (combined, excluded) and generated initial themes and categories in consensus with 2nd investigator	2
4	Finalized themes and categories in consensus with 2nd investigator (refined, combined, split)	2
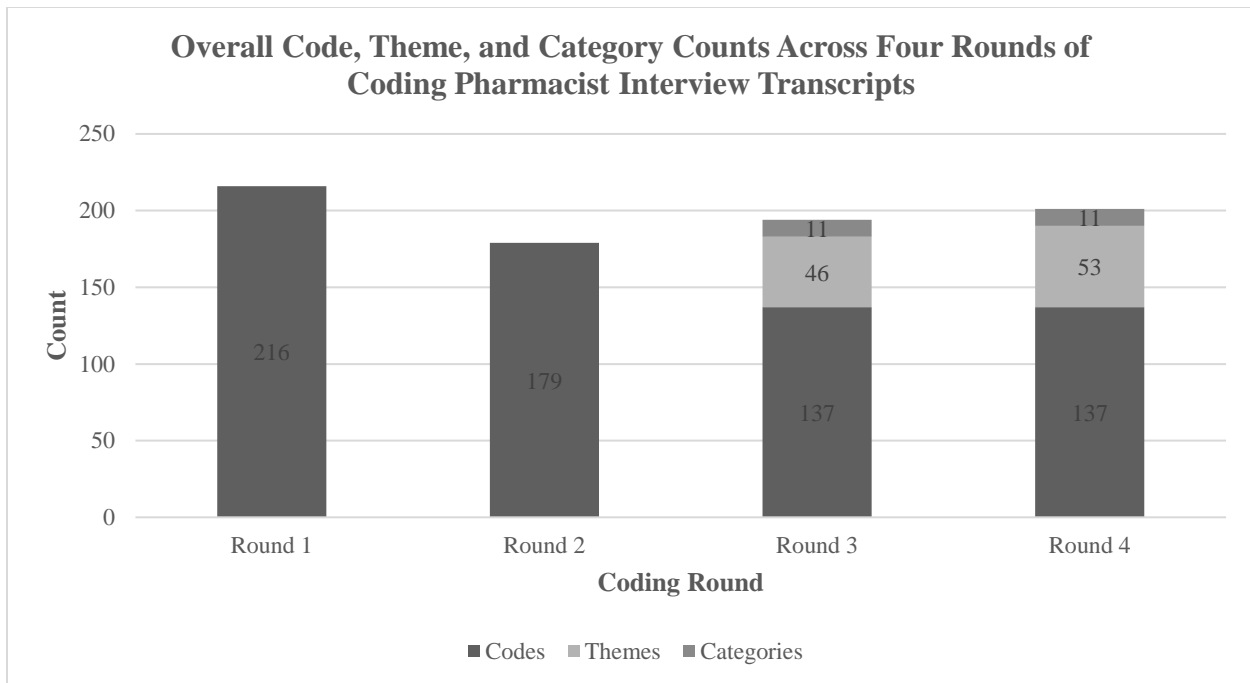
Figure 4.1 Overall Code, Theme, and Category Counts Across Four Rounds of Coding Pharmacist Interview Transcripts

Overall, 53 themes amongst 11 categories were identified within pharmacists' discussion of pharmacy-based naloxone services in Alabama (Table 4.5). Discussion was grouped into the following 11 broad categories: 1) training needs; 2) attitudes; 3-5) individual, organization, and external-level barriers; 6-8) individual, organization, and external-level facilitators; and 9-11) current naloxone service implementation strategies, specifically workflow, marketing, and communication strategies. Barriers and facilitators were sub-divided into individual-level, organization-level, and external-level based on Greenhalgh (2004).[292] Likewise, current naloxone service implementation strategies were sub-divided into workflow, marketing, and communication strategies based on Waltz (2015).[293]

Table 4.5 Categories Identified from Pharmacist Interviews

No.	Category	# Codes	# Themes
1	**Training Needs**	**24**	**3**
2	**Attitudes**	**16**	**3**
	Barriers	**33**	**14**
3	Individual-Level	13	6
4	Organization-Level	9	5
5	External-Level	11	3
	Facilitators	**39**	**16**
6	Individual-Level	9	5
7	Organization-Level	24	9
8	External-Level	6	2
	Current Naloxone Service Implementation Strategies	**27**	**17**
9	Workflow	11	8
10	Marketing	7	4
11	Communication	9	5

The following sections will describe the themes identified from pharmacist interviews according to broad categories: training needs, attitudes, barriers, facilitators, and current naloxone service implementation strategies.

4.1.2.1 Training Needs, Attitudes, Barriers, and Facilitators

Themes were identified in the following broad categories: community pharmacists' naloxone training needs (3 themes); attitudes regarding pharmacy-based naloxone services (3 themes); barriers to pharmacy-based naloxone services (14 themes); and facilitators to pharmacy-based naloxone services (16 themes). Frequencies of themes across transcripts are reported below (n).

Training Needs

Three themes were related to training needs (Table 4.6), and the most frequently cited theme was misinformation or lack of training regarding basic naloxone facts (n=56). Reflecting

this, community pharmacists expressed unawareness of where to find the Alabama statewide standing order for naloxone, state-specific legalities for dispensing naloxone, and dosing and administration information for the various dosage forms. In fact, one pharmacist stated that *"All I had training on was…the Narcan [nasal spray], not the shot."* Pharmacists also preferred live, interactive training formats over home-study or static formats (n=37). Furthermore, pharmacists expressed a lack of training regarding communication strategies (n=21), as exemplified by one pharmacist stating, *"...I'm not comfortable telling the patients that they've gotta do this [purchase naloxone]. I don't think that I've been trained enough to do that."*

Table 4.6 Community Pharmacists' Training Needs Regarding Pharmacy-Based Naloxone Services (10 Pharmacists)

Category	Theme	n[a]	Representative Quote
TRAINING NEEDS (n=114)	Misinformation or lack of training regarding basic naloxone facts	56	"I think everyone needs to be aware that Alabama Department of Health has that protocol…I think that's the first thing, educating the pharmacists that okay, this is where you can go, this is where the protocol [state-wide standing order] is." (P4) "…it's important to know who can dispense it, how to dispense it…and what's legal in your state." (P2) "I don't know what the law is for, but I know we don't dispense it [naloxone] without a prescription. We only dispense it with a prescription." (P2) "I…need a refresher on the different products available and their dosing…" (P3) "I know that you can get it [naloxone] without a prescription, but I really don't know the rules or the laws on it. I asked a couple of my coworkers, and they told me the same thing. Like, 'You know, I really don't know.'" (P4) "All I had training on was, well not training. But all I've looked into was the Narcan [nasal spray], not the shot." (P10) "I feel comfortable in dispensing it [naloxone]…I can educate a patient on drawing up a vial or the use of Narcan nasal spray or whatever. I don't feel uncomfortable. It's the, I guess the steps before the dispensing that I probably need more education there." (P1) "…at what threshold do you really consider, hey, they need to have a naloxone at home, in their car, whatever for a pain management patient?" (P5)
	Preference for live, interactive training formats vs home-study or static formats	37	"I think three hours would be great… An hour may cover it [training] but it's a lot to learn about it [naloxone]." (P2) "…we actually did a course around here. It was actually like a dinner event…" (P2)

			"I would say [prefer] either a live webinar or in person [training] so that you can go over each drug, how it's supplied, how it comes and the steps to train somebody on it." (P6) "I think [prefer] a live webinar, live CE maybe with a lab with it. You'd actually have practice drawing it [naloxone] up, class administrations, and do the whole technique thing. Then maybe even act out certain scenarios, like this would be where you would use examples." (P7) "…maybe as a company, we could do just as we do CPR training, mandatory every three years, two years. Why not have naloxone training or maybe even more of them. Maybe have Naloxone/Epi-pen, or epinephrine, or if you didn't want to devote a lot of time into one area, maybe combine a patient safety type thing... have classes to practice with the atomizers or the IM's." (P8)
	Lack of training regarding communication strategies	21	"How do you talk to someone? How do you approach them about talking to them about a drug that counteracts abuse...?" (P10) "How to tell them [patients] how to use it [naloxone] is important to know. How to educate the family." (P2) "If someone is willing to take it [naloxone], we haven't had that many extended conversations." (P8) "I feel comfortable with standing prescriptions [Alabama's statewide standing order] dispensing it [naloxone], but I'm not comfortable telling the patients that they've gotta do this. I don't think that I've been trained enough to do that." (P4) "What do we do once we identify these patients that are possibly abusing this [opioids]?" (P5) "…you need to be careful because are you [the pharmacist] insinuating that I'm [the patient] going to try and overdose on this and this is going to save my life versus why do you think I would need to have this?…You would almost feel like you were judging them, and you would have to explain why you feel like they need this [naloxone]. So that's pretty tough…" (P6)

[a]n=frequency with which the theme/category was coded across transcripts

Attitudes

Regarding pharmacists' attitudes towards pharmacy-based naloxone services, 3 themes were identified (Table 4.7). Positive discussion supporting pharmacy-based naloxone services (n=37) was more frequent than negative discussion not supporting this service (n=18). Pharmacists in support of pharmacy-based naloxone services discussed the benefits of the service in terms of the potential to save lives in their community and society in general, fulfilling their professional duty to help patients and applying more of their education in practice, and setting their pharmacy apart from others. This is exemplified by one pharmacist stating that pharmacists have too much education to *"let people slip through the cracks."* Another pharmacist supported naloxone services in order to *"ease the stigma for patients who have legitimate pain...and protect society,"* while another wanted to offer naloxone services before their pharmacy competitors in order to have a competitive advantage.

On the other hand, pharmacists also discussed lack of support for or downsides regarding pharmacy-based naloxone services (n=18) in terms of a negative impression of individuals with opioid use disorder and the belief that naloxone provision is more appropriate in the physician practice rather than pharmacy setting. For example, one pharmacist stated that bringing individuals with opioid use disorder into the pharmacy may disrupt business and *"opens a Pandora's box of problems,"* while another mentioned the belief that providing naloxone to everyone in need will negatively impact societal healthcare costs. Another believed that naloxone services were *"better off in a personal doctor-patient relationship."*

However, community pharmacists were confused about their roles and responsibilities as part of this service and how they fit in with other professionals and patients (n=37). In fact, one pharmacist stated that *"pharmacists need to be educated on their scope as far as what they can*

114

do and what they can say." As mentioned above, some pharmacists believed that naloxone

services were the purview of the physician rather than the pharmacist, and attributed the

responsibility for opioid misuse and abuse to the physician, notably pain clinics. In the context

of this perceived physician over-prescribing of opioids, pharmacists felt stuck between physician

prescribing practices and federal agency dispensing regulations. Other pharmacists held a

different view, attributing responsibility for opioid misuse and abuse to the patient, stating that

"drug addicts…never think they're the problem" and further suggested that it's the patients'

responsibility to make choices regarding their opioid therapy.

Table 4.7 Community Pharmacists' Attitudes Regarding Pharmacy-Based Naloxone Services (10 Pharmacists)

Category	Theme	n[a]	Representative Quote
ATTITUDES (n=92)	Supports pharmacy-based naloxone services	37	"We got too much education to let people slip through the cracks, and then you end up failing people too." (P2) "I'm going to talk to some people from my higher ups too because it would help out communities like a lot of communities in Alabama and the South, which is so heavily filled with narcotics and people overdosing. Naloxone would definitely save their lives." (P2) "We've lost people that we deal with and customers to overdoses. It [naloxone] can be a life saver if they'd only been educated on it." (P2) "It's [naloxone] not our cheapest medicine, but it's not the most expensive either. So it's not something I mind having on our shelves. So it's probably nice to have on our shelves." (P1) "A couple of the pharmacists and myself, we looked at ways to maybe use this [naloxone services] as a way to set ourselves apart from some of the other pharmacies and to offer something like this before others did." (P1) "I just feel like the whole opioid epidemic is such a huge deal, especially here where I live. We're in the number one county in the state and like top five or six counties in the nation, and it touches every family. I just feel like we're [pharmacists] such a tiny little part of it, but if we can do anything to mitigate that then we need to. That's why I wanted to do this, because if I can do anything to help to reverse this trend." (P5) "I guess the reason for prescribing it [naloxone] is not always for the patient. It's for society..." (P9) "I would totally support that regulation [pharmacy-based naloxone services]. I would definitely support it because I think that that maybe could ease the stigma for patients who have legitimate pain, and would protect society as a whole in some fashion, hopefully." (P9)

| | Role confusion and conflicted view of responsibilities | 37 | "...what are our roles, our scope of practice as far as these things [naloxone]?" (P5)

"I think more pharmacists need to be educated on their scope as far as what they can do and what they can say, dispensing it [naloxone] and everything." (P5)

"Oxycodone, 30 milligram and over 120...that prescription is gonna be filled somewhere. It's just their [the patients'] choice not to fill it." (P1)

"…so many people that are on C2's [opioids] and they're on them for the fact that the doctor just won't stop writing them for them and then they get addicted to them." (P2)

"They'll say ... all those drug addicts... "Well we can't get our medicine." …they never think they're the problem." (P7)

"…the location that I've worked at is I guess you could say a rougher area…We certainly have some controlled substance issues, certain prescribers that tend to over-prescribe and so from that point of view it's definitely a challenge. Trying to work through each patient and trying to think about should they really be on this…" (P8)

"I see patients frequently who say that they don't have a doctor that will prescribe their medicine for them, and ask where can they go. Then, the DEA doesn't want a pharmacy to fill a prescription that's not from our local area. If there's no local area doctors, then where are the patients supposed to go?" (P9)

"…known doctors in the area…you just get to know them. But you see prescriptions all day long for the same items [opioids]. The same medications. You just kinda learn who those doctors are and ... and if they're not necessarily a pain management doctor or an orthopedic." (P3)

"…with the increase of pain clinics, and them letting them [patients] have early fills, and then just to access to the pain clinic. I feel like maybe that's why it's [opioids] overprescribed." (P4) |
| | Does not support pharmacy-based naloxone services | 18 | "I don't necessarily know that I agree 100% with the standing orders simply because I think it needs to be a conversation between the doctor and the patient. If |

| | | the doctor feels like this patient should have this onboard or a family member should have it onboard, then he should write a prescription for it. I think that's better off in a personal doctor-patient relationship." (P6)

"I just don't know about opening it [naloxone] up to everyone and we [pharmacists] should offer it because you're giving a $500 medication to somebody that might just throw it somewhere and lose it or forget it or whatever and then there goes your increased healthcare cost." (P6)

"So if you take on one of those patients [individuals with opioid use disorder] you're gonna have 20 more come in in a week because they're all coming at you and start coming in. And that just opens a Pandora's box of problems." (P5)

"…either we're going to use them [opioids] as a tool to treat patients past pain, or we are going to take them off the table and try to protect society from addiction. You can't have both things." (P9)

"Not that I wouldn't want someone to have it [naloxone] in their home if they needed it. I honestly don't care, but I'm happy for them to have it. You know what I mean?" (P9) |
|---|---|---|

[a]n=frequency with which the theme/category was coded across transcripts

Barriers and Facilitators

Fourteen themes related to barriers to pharmacy-based naloxone services implementation were discussed (Table 4.8) and categorized as individual-level (6 themes), organization-level (5 themes), and external-level (3 themes). Regarding facilitators (Table 4.9), 16 themes were discussed and also categorized as individual-level (5 themes), organization-level (9 themes), and external-level (2 themes). Individual-level barriers (n=143) and organization-level facilitators (n=161) were the most frequently discussed across all transcripts.

Barriers

Individual-level barriers included 6 themes (Table 4.8). The most frequently cited theme was perceived resistance from patients (n=46). This is reflected by one pharmacist saying, *"they think they are not at risk of overdosing and just refuse it [naloxone],"* while another pharmacist mentioned a perception that patients think pharmacists are judging them by offering naloxone. The perceived high cost of naloxone for patients (n=42) was also commonly discussed. One pharmacist stated that any naloxone co-pay above $15 was cost prohibitive for patients, while another believed that the large discrepancy in price between opioid prescription medications at a $1.60 co-pay and naloxone at a $140 co-pay was a barrier for patients. The next most frequently discussed themes were feeling uncomfortable approaching or communicating with patients regarding opioid use or naloxone (n=20) and concern that providing naloxone increases opioid use (n=18). In fact, one pharmacist said, *"it's just hard to have that conversation [about opioid overdose risk] with people. I feel like if it originates from the doctor it is a little more well received."* Another pharmacist mentioned feeling like they were judging the patient by discussing naloxone. The least frequently mentioned themes were fear of professional consequences (n=12) and perceived low demand for naloxone (n=5).

Organization-level barriers included 5 themes. The most frequently cited theme was lack of time in the pharmacy (n=23), with one pharmacist stating that sometimes they could not even spare 5-10 minutes to counsel a patient about opioid overdose risk and naloxone. Furthermore, pressure to comply with corporate culture and protocols (n=14), difficulty contacting prescribers (n=13), and naloxone not being kept in stock or problems stocking it (n=13) were also discussed as barriers to naloxone services implementation. One pharmacist mentioned that independently-owned pharmacies would have an easier time implementing naloxone services compared to corporately-owned pharmacies due to less time- and effort-restrictive policies. Others voiced frustration that *"doctor[s] will probably not care, if you reach out to them"* about the need for naloxone and not keeping naloxone in stock due to the limited expiration date (typically one year). Lack of access to patients' medication history/EMR was the least frequently discussed theme (n=2).

External-level barriers included 3 themes. The most frequently cited theme was insurance coverage issues (n=36), followed by pressure to comply with regulatory agencies, laws, and regulations (n=33). Pharmacists discussed frustration with seeing prior authorizations for naloxone, or with coverage under Alabama Medicaid being limited to 5 drugs including naloxone. They further described pressure due to DEA presence in the local area, as well as restricted allotments of opioids available from pharmacy wholesalers negatively affecting their business. The least frequently cited theme was a climate of stigmatization and sensationalism (n=12), which negatively impacted pharmacies' provision of legitimate opioid prescriptions by propagating a culture of suspicion, and contributed to pharmacists' reluctance to provide pharmacy-based naloxone services.

Table 4.8 Community Pharmacists' Individual, Organization, and External-Level Barriers Regarding Pharmacy-Based Naloxone Services (10 Pharmacists)

Category	Theme	n[a]	Representative Quote
BARRIER: INDIVIDUAL-LEVEL (n=143)	Perceived resistance from patients	46	"…we would love for more patients to get it [naloxone], but most…are quite resistant to getting it. They feel like they don't need it. They know how to take their medicine and they think they are not at risk of overdosing and just refuse it." (P1) "Yeah, so we were selling two vials [of naloxone] and two syringes and two alcohol pads for $39.95. Even at that price, people just didn't want to spend $40, because they felt like they didn't need it. That's the biggest resistance that we've seen is that "I won't pay too much. I don't need it." So that's our obstacle. People thinking that it's for somebody else." (P1) "…some people…especially the elderly…their mindset is that they've been taking it [prescription opioid] for awhile, they're not going to have any incident, they're not going to OD." (P2) "…a lot of people that come in…they're on the defense because they've been turned down by many places or people. They think people pass judgment on them and even talking to them sometimes is even stressful for them." (P2) "A lot of them [patients] have been on, you know, a certain amount of opioids for an extensive amount of time and they probably wouldn't think that they're at risk of overdosing." (P4) "…most people want their medicine free." (P7)
	Perceived high cost of naloxone for patients	42	"I think if…Narcan had a more affordable copay, even the people resistant to it may be willing to spend a little bit of money just to have it on hand. I think that's the biggest barrier to people getting it. Especially at some of our poorer stores…But if a Narcan nasal spray had affordable copay at $15 or less, they would do that." (P1) "I guess the biggest difficulty is cost. I think people would get it if it wasn't so expensive." (P2)

			"I do remember it being really expensive for the patient, whereas their Oxycodone co-pay is $1.60, and I think that their Naloxone co-pay was like $140 or something." (P9)
			"And thankfully it [naloxone] was covered on Medicaid, which was huge because if it wasn't, they would've never gotten it." (P4)
	Feeling uncomfortable approaching or communicating with patients regarding opioid use and naloxone	20	"Some people take it as an insult that you're telling them that they need this [naloxone] as a rescue…" (P2) "…you really walk them [patients] through with a fine tooth comb. It's hard, the way you talk to them, and the way you express it all. 'This [naloxone] is just to help you. I'm not passing judgment on you or saying that you're going to take too much of it.' I think…communication is a barrier with it [naloxone]." (P2) "Well, to avoid argument, I guess I would just say that I don't have it [prescription opioid] in stock." (P4) "…it's just hard to have that conversation [about opioid overdose risk] with people. I feel like if it originates from the doctor it is a little more well received." (P5) "You would almost feel like you were judging them, and you would have to explain why you feel like they need this [naloxone]." (P3) "At least from where I work and what I see is a lot of pharmacists don't take that time to try to step in and say something." (P6) "…how to approach a customer. You don't want to make them feel like they're possible abusers or something like that. That's one of the main ... How do you talk to someone." (P10)
	Concern that providing naloxone increases opioid use	18	"I'm a little concerned that this [providing naloxone] is going to turn into a situation of let me overdose and feel how that is so you can bring me back. So it would turn into almost a game that young adults might play." (P3)

122

			"…you just run the gamut of people that say well, we're just encouraging people if we give this [naloxone] out along with it [opioids], or maybe we're not helping them really in the long run." (P6) "…those conflicts may be internal with some people that they're like 'I'm not going to do this [provide naloxone] because it's just promoting.'…You've got that age old conflict there." (P6)
	Fear of professional consequences	12	"HIPAA regulations prevent you from discussing a lot of things with the patient's family who really need to know about the signs and symptoms of opioid abuse. But a lot of pharmacists are scared to cross that line for fear that "Oh gosh, if I talk about opioid abuse here, if I say this patient's abusing, what will the HIPAA police come and do to me?" (P1) "And too, we just have some doctors we refuse to fill for. And I know that you're really not supposed to do that, doctors have called and told us they'd sue us for defamation, and in that case we'll just tell the patient we don't have this drug or we can't fill that drug today and leave it at that." (P5) "…I have personally seen the DEA take control of the practices and close down street offices, including a pharmacy" (P7)
	Perceived low demand for naloxone	5	"…it [naloxone] wasn't something that we were dispensing every day and not something that every opioid patient wanted." (P1) "They [patients] didn't really care to get it [naloxone]…" (P4) "I haven't seen a prescription for it [naloxone]. And doctors certainly, they don't push it in the area…" (P4) "It's not that they would not carry it [naloxone] regularly if the demand was for it, it's just like I said, most patients when we have had prescriptions for it, they have been very defensive and said, 'No, don't order it.'" (P8) "It's [naloxone] just not very prevalent here now." (P3)

BARRIER: ORGANIZATION-LEVEL (n=65)	Lack of time	23	"I think time constraint would be a big deal in the change as far as counseling them [about naloxone]." (P2) "When you're doing 300, 400 scrips a day, you can barely get that [providing naloxone] in." (P2) "…the PDMP…That needs to be easily accessible and quick and easy to use because usually pharmacies are under a ton of pressure to just get through things quickly." (P9) "…opioid counseling I would say between five and 10 minutes depending on who I'm talking to. Sometimes I just can't do it…or I'm interrupted or the person is not there…most people come during times where I can actually spend five minutes, 10 minutes. Every once in a while, I can't get to it." (P10)
	Pressure to comply with corporate culture and protocols	14	"…our company basically told us to limit the amount of controls that we fill because our ratio was too high, the ratio of maintenance drugs to control drugs." (P2) "I think the independents [independently-owned pharmacies] would be very receptive of it [providing naloxone]. I think you would have a harder time with chains…because they're already getting bombarded…You get bombarded with so much stuff from corporate, and they change, that you barely have enough time to do that let alone any additional requirements that the state or the FDA or the DEA tries to enforce as well." (P8) "We only dispense it [naloxone] with a prescription…That's for my store's policy, from my headquarters." (P2)
	Difficulty contacting prescribers	13	"But if I have to search down a prescription [for naloxone] in the process of filling a prescription that would take up too much time. To have to call a prescriber, and get authorization." (P7) "You know how in our [opioid] consultations there's a part where if we see any red flags with other medications that they're on like benzodiazepines, we can contact the doctor for them. Which we have done in the past, but no MDs really,

			maybe a couple have changed their medication list, but that is one thing where even sometimes when we get doctors to try to change from one to another or take out something, it's hard to get in touch with them." (P10) "…there's not much you can do. The doctor will probably not care, if you reach out to them." (P4) "Some of the pain management people, they don't write it [naloxone]. They won't give it to them [patients]." (P2)
	Naloxone is not kept in stock or problems stocking it (expiration date, cost)	13	"The only thing I can really think of is that I won't be able, especially due to the price, I wouldn't necessarily be able to say, hey I've got it [naloxone] right there. Let me give you some. I'd have to order it because those injections, I mean they're $4,000." (P4) "No, I don't have any [naloxone]. I mean I'm able to order it and it be in the next day." (P4) "Usually we just keep the vials of it [naloxone] because it's always cheaper and I don't want to have 130 dollar bottle of Narcan on the shelf for six months that nobody ever gets." (P5) "No, we don't keep it in stock. We have to order it." (P3) "…most of the ones [naloxone] we've gotten in have only had about a year's dating [expiration date]…You want to make sure it's within date." (P6)
	Lack of access to patients' medication history/EMR	2	"…we don't see their medical records so we don't know what they're legitimately being treated for…So if anything comes up we just have to use our best judgment to question it and research it." (P5) "We're right at the corner of Alabama, Mississippi, and Florida, and we're really close to all of them. We're right in the triangle… Our Alabama data bank [PDMP] can't see…anything they were doing or what they had filled [outside of Alabama]." (P2)
BARRIER: EXTERNAL	Insurance coverage issues	36	"I think that it would benefit the community if insurance companies would just cover Naloxone the same as they cover other medicines, so like if they have a

ENVIRONMENT (n=81)			copay or whatever. There should never be a PA [prior authorization] needed for Naloxone." (P9) "…we can't control how insurances bill and the reimbursement and what those copays are. Obviously we don't have a big play in that…I have seen a couple of insurances have gotten really strict here lately…The DUR [drug utilization review] codes have gotten a lot more strict…" (P8) "…it [naloxone] was part of the Medicaid five, how those people can only get five prescriptions a month. So if it took up their five spots, they definitely wouldn't get it." (P4)
	Pressure to comply with regulatory agencies, laws, and regulations	33	"Regulations to stop doctors from prescribing so much [opioids] has done nothing to stop abuse. It's even, in my opinion, as the laws and regulations have probably made it worse in that people that can't get it prescribed anymore are turning to street drugs and it's a problem." (P1) "…only 5% of your dispensing can be narcotics. So you have to have a certain balance of non-controlled substances to controlled substances or you'll be cut off from ordering the controlled substances." (P4) "And here in [this] county we're kind of in a unique situation, in that in the past I'm gonna say 20 years we've had a fair amount of DEA involvement in physician prescribing practices." (P7) "We order from [name of wholesaler] and one of the restrictions we have is that in order to order a certain amount of narcotics you have to be dispensing a certain amount of non control. So [the wholesaler] likes to keep the ratio around 24% control to non control." (P7) "I don't think that pharmacists don't know. I think that it's the climate, like the environment that we're in where it's like there's so much pressure here on physicians to not prescribe it [opioids] because the opioid crisis." (P9) "It's like kind of a slippery slope, though, because the whole thing about it [naloxone] being prescription only, and it's for the intended patients…The

			regulations would have to change entirely, really, just for society to benefit." (P9)
	Climate of stigmatization and sensationalism	12	"I think the most thing that we need is kind of re-trained as far as being judgmental of people because that's the hardest thing. It was for me for a long time. Someone walks up and you say you can tell what they want without knowing that person's story. I think we all become kind of immune to them after awhile, but you have to really, really be trained as far as treating people right." (P2) "Most people…know the doctor will pull them out the [opioid] program and the pharmacy will inform if they're a problem." (P5) "So many people, so many pharmacists ... I know people get really jaded and it's hard not to." (P8) "I think that there are patients who are legitimately pain who are not receiving treatment, or are being stigmatized when they shouldn't be. I think people who are in pain should be receiving treatment for their pain." (P9) "So I think everybody here [at the pharmacy] is taught to be on extreme guard for any type of misuse and I think it's because of the things we've seen happen here…we even had practitioners writing Methadone for pregnant moms and methadone for the mom and for the partner…That one physician did lose his license. So I think that might have played into it [being on guard]." (P7)

[a]n=frequency with which the theme/category was coded across transcripts

Facilitators

When asked about facilitators to pharmacy-based naloxone services implementation, we discovered 5 themes within the individual-level facilitators category (Table 4.9). The most frequently cited themes were using communication strategies with patients and prescribers (n=27), building personal pharmacist-patient and pharmacist-prescriber relationships (n=26), and fostering a sense of professional duty (n=23). For example, one pharmacist said, *"We have a good faith dispensing policy...Our stance is number one communication,"* and *"[Our pharmacy] has really pushed us to try to open those doors to conversations, say let's try to work with your doctors..."* The least frequently cited themes were learning from personal stories/anecdotes of others i.e. social comparison (n=14), and promoting pharmacists' sense of autonomy/authority (n=6).

Organization-level facilitators included 9 themes. The most frequently cited theme was resources/technology to support identification of eligible patients (n=83), followed by creating a pharmacy protocol for providing naloxone based on pharmacy staff input (n=55). For example, pharmacists discussed the use of the PDMP in supporting opioid and naloxone related counseling decisions, with one pharmacist also stating, *"It would be nice if maybe just the computer would flag you on certain patients."* Having a readily available method to solicit recommendations from prescribers (n=16), corporate/clinical support (n=14), and utilizing marketing strategies (n=11) were discussed with moderate frequency. The least frequently discussed themes were finding more affordable options for patients (n=5), having readily available resources for patients (n=5), establishing a leader/champion in the pharmacy (n=2), and ensuring an appropriate physical setting (n=1). In terms of finding more affordable options for patients, pharmacists mentioned manufacturer discount coupons for the Evzio® auto-injector, and offering the vial of

naloxone for intramuscular injection plus syringe instead of the more expensive Narcan® nasal spray.

External-level facilitators included 2 themes. The most frequently cited theme was advocating for national or state-wide policy changes (n=15). As part of this theme, pharmacists discussed collaboration between the Board of Pharmacy and other pharmacy organizations in making a statewide naloxone continuing education program, and one pharmacist mentioned *"making [naloxone] part of a REMS [Risk Evaluation and Mitigation program."* The least frequently cited theme was promoting local and community partnerships (n=3), with one pharmacist discussing partnering with the local police department for education purposes and another promoting community health fairs in the pharmacy to allow a time for patients/caregivers to come in and ask the pharmacist about naloxone.

Table 4.9 Community Pharmacists' Individual, Organization, and External-Level Facilitators Regarding Pharmacy-Based Naloxone Services (10 Pharmacists)

Category	Theme	nᵃ	Representative Quote
FACILITATOR: INDIVIDUAL-LEVEL (n=77)	Using effective communication strategies with patients and prescribers	27	"I know that if we talk to them [patients], that's the number one. I think maybe if the doctor talked to them." (P2) "I think it's a big stigma too because the physicians will give them [patients] so much of a medication [prescription opioid] and they don't let them know what could possibly happen to them by taking so much, about the respiratory distress. I think that's a big barrier. I think the biggest way to solve it is to communicate with them." (P2) "I think honestly just a face to face conversation would help, I think you would just have to have a team approach and disciplined approach to actually do it for each patient." (P5) "I think they [physicians] need to tell them [patients] at the appointment, hey, this is a new protocol [naloxone statewide standing order] that the state is starting to enact. We're doing it for your safety. We know you've been on this medication [prescription opioid], we know you know how to take it. However, any reaction to any drug no matter what it is can happen at any point of the patient taking it. That could be allergic reactions or anything." (P8) "Number one, if it's a brand new patient to that type of medication [opioid], I'll try to at least have a conversation. What's going on? What's happened? I've had surgery or whatever the situation is, try to dig into that." (P6) "…the challenge with that is I think a lot of people overestimate, you know, 'I'm not going to have a problem with this medication [opioid]. I'm not going to get hooked. I'm not going to be the one.' Whatever you want to say. I've heard the gamut of all explanations or things that people might say regarding it. It's opening that window to just talk to them, and just lay out the facts about it, and the concerns." (P6) "[Our pharmacy] has really pushed us to try to open those doors to conversations, say let's try to work with your doctors. There's some ways that

			maybe you can either back down on the dosing and also to try to work towards maybe getting off of it [opioid]. Is there an underlying issue that can be addressed, whether it's some kind of surgery that's needed, et cetera, et cetera." (P6)
			"We have a good faith dispensing policy which most big chains and stuff do have some sort of policy regarding that. Our stance is number one communication. We do have some stances as far as everything is individualized. That's one thing. Some of the other companies, at least what I've heard, they may just be more stop here. You can fill this. You can do this. Very regimented. The big thing now is seven days worth of an opioid if you've never had one. [Our pharmacy] doesn't really have that stance. It's simply everybody is individualized and the number one thing is just communication." (P6)
			"I kind of just say what is this person's situation? Let me communicate with them, see what's going on and kind of go from there. The company [pharmacy], they recognize obviously there's a problem, but their number one guideline is just the communication part." (P6)
			"…when people start a fentanyl patch...I'm like… 'You can stop breathing with this medicine…You need somebody watching you to get you help, if you need help.' And they don't really take it seriously. That's why I scare them sometimes, cause I'm worried for them." (P7)
			"We also have that standing order for the Narcan dispensing that we keep just in case anyone does want it. We've let them [patients receiving opioid counseling] know that we do offer it in case it is something they want to have on hand." (P10)
	Building personal pharmacist-patient and pharmacist-prescriber relationships	26	"That's a good thing about small community pharmacies is that people have a trust in you. If you tell them, they're like well since you put it like that. I know you wouldn't do anything to hurt me. You're not passing judgment on me." (P2)
			"Because our pharmacy is so small, we just try to set up the relationship that we know them [patients]. You know that person. You know their name so they feel a little bit more comfortable talking. I think if it's changed you just can't get

			that. They won't really listen to you because they don't feel like they know you." (P2)
			"So most of the time it's a good relationship [between the pharmacy and the physician's office]…But sometimes if you don't know the nurses they'll get a little combative, like you're trying to keep their patients away from the medicine, and that's not always the case, it's just you're trying to do the right thing." (P5)
			"I'd be glad to talk to the doctor, maybe call them up, see if there's some other options. Maybe they can ... come up with a plan. More of that collaborative type practice." (P6)
			"…if you're honest with people or you're honest with the physicians and you're honest with patients, then we have a team-building thing where we can maybe actually help people." (P9)
			"I expect the physician who his patients come to me, we're partners in their care, I expect them to be supportive of that also, or that would be a red flag in my opinion." (P9)
			"Yeah and a lot of these patients that I have counseled, I've known for about three years now. It's not like I'm someone brand new telling them to get something." (P10)
	Fostering a sense of professional duty	23	"So it's not every day that you get to save someone's life." (P1)
			"We [pharmacists] got too much education to let people slip through the cracks, and then you end up failing people too." (P2)
			"You're [pharmacists] supposed to be helping everybody." (P2)
			"I know it's [naloxone] needed out there and I feel like I can adequately help them [patients], and adequately tell them how to use it…make it easier access for them too, because…a lot of the pain management doctors don't even write it [prescribe naloxone]…" (P2)

			"I just feel like the whole opioid epidemic is such a huge deal, especially here where I live…it touches every family. I just feel like we're such a tiny little part of it, but if we can do anything to mitigate that then we need to. That's why I wanted to do this, because if I can do anything to help to reverse this trend." (P5)
			"I think the main thing is if you can save a life if someone accidentally overdoses more so than just strictly a drug addict, if you will, that's really pushing the limits, but someone that accidentally...that's a good thing to try to save a life there possibly with the naloxone." (P6)
			"…you have a lot of people that maybe accidentally they took double the dose [of prescription opioid], they didn't realize it, and then something could happen. To me, that's the number one good intention of it [naloxone]." (P6)
	Learning from personal stories/anecdotes of others (social comparison)	14	"That story's been told company wide. So around our team, most people know why we stock it [naloxone] and the advantages of stocking it." (P1) "It's available as a pen in all of our stores and we actually have one of our pharmacists save a guy's life by having Naloxone on hand." (P1) "…the last eight years, every single year has been worse and worse. We hear about some of our patients OD'ing on narcotics because they've taken too many." (P2) "I've had a friend, he's in [city in Alabama], he had somebody drop a person in an overdose at his door at the pharmacy. Give the pharmacist a plan of what to do if that happens. One, two, three, four. I think that would make everybody feel more comfortable about it." (P5) "I had a personal story with someone that had actually…overdosed in our restroom at our store. They were filling an opioid and a benzo combination…About an hour later they found her. It was too late to do anything…that one kind of hit home as far as it's a real problem." (P6)
	Promoting pharmacists' sense of autonomy/authority	6	"I don't want to fall back on, 'It's the law.' I want to have ethical compassion and be able to have my own discernment as far as the needs of the patient, rather than having a million laws limiting it." (P9)

133

			"…if there was a way that you knew you could write the [naloxone] order yourself, that would take another huge thing down because chasing down the doctors sometimes is time consuming and if we just had some autonomy there or prescribing privileges." (P7) "You're going to have some pharmacists that are going to be much more strict. Their belief may be nobody should be on an opioid ever…Some people say it's up to the doctor. If they want them on it just go with it. Me personally, I'm more towards the middle." (P6)
FACILITATOR: ORGANIZATION-LEVEL (n=161)	Resources/technology to support identification of eligible patients	83	"Identification would be a big one. Perhaps I would work with some of the opioid prescribers in identifying patients and making sure those patients are well educated on the advantages of having Naloxone in the home." (P1) "New patients, the PDMP will be checked or if a patient is willing to pay cash for a prescription…" (P1) "Yeah I think that's something, you know having a standing order on hand would be a great tool, just to have right there in every pharmacy so you don't have to go searching for it and you're just prepared." (P3) "It would be nice if maybe just the computer would flag you on certain patients." (P5) "The use of the national database, the prescription database [PDMP], helps a lot." (P6) "…what we can do is put an internal block on it so that [opioid] prescription can't be sold without us at least counseling them on that. That's the good thing within our system that if you want to stop it from being sold before you talk to them…then you can have that option." (P6) "Last week we started doing the opioid counseling that pops up in one of our central locations. Our affiliate has a list of names…That's when we first started counseling patients who have already been on it [opioid], not just new patients." (P10)

	Creating a pharmacy protocol for providing naloxone based on pharmacy staff input	55	"…if it's a new patient we have to get maintenance medicine for them, not just controlled substances. With it they have to fill something else besides just that [opioid] because it throws the quotient off if that's all they're getting…" (P2) "Maybe just having a formal protocol, like if you give one dose obviously you need to call 911…" (P5) "They [this corporately-owned pharmacy] leave a lot to the pharmacists which I think is good versus just a heavy handed, here's seven days worth [prescription opioid], and that's it..." (P6) "Our internal policy is if someone is over 50 MME's, morphine milligram equivalents, if they are taking therapy that is above that, we should offer naloxone just simply obviously as a safety thing." (P6) "I always make everybody get everything…if you have a prescription for naloxone you have to buy it before I'll sell you your oxycodone or whatever." (P9) "We do have a printout that we use that stands as pretty much a hard copy. It's got a couple questions…that's just part of the standing order that we got from the…website." (P10)
	Readily available method to solicit recommendations from prescribers	16	"I think maybe if the doctor talked to them [patients]. Some of them come in and it's hard because they have no idea why the doctor didn't say anything. They don't know. They think sometimes maybe it's [naloxone] like another narcotic or pain medicine, so they don't have a clue as to why they're getting it." (P2) "…if you could get doctors on board to make, you know if their patients wanted to get their opioids for the month, if they could also have to get naloxone with it at least one time, then that would, you know force it to go into homes." (P4) "…if we had some kind of document we could fill out and fax to the doctor saying, 'I have administered this or I've just sent this [naloxone] to the patient so they can administer at home if needed. This is just documentation for your records too.'" (P5)

			"…usually almost always what we do is just call and leave a message with a nurse, or secretary, or receptionist…We actually have the doctor himself, when he gets a minute, trying to be respectful of their time, but when he gets a minute we just want to discuss this patient's therapy, and maybe if there's some options that are out there that are available for other things, and going from there. So, number one thing is just reaching out like that." (P6)
	Corporate/clinical support	14	"We have a couple clinical pharmacists that run clinical programs with our pharmacy…I think that we could get support. They're just only a phone call away." (P2) "Obviously our company [corporately-owned pharmacy] will back us up with whatever kind of judgements we try to make." (P6) "My thought would be, I think, even maybe as a company, we could do just as we do CPR training, mandatory every three years, two years. Why not have naloxone training or maybe even more of them. Maybe have Naloxone/Epi-pen, or…combine a patient safety type thing. That would be based on the company…" (P6) "Internally we do have some computer training. I'm sure most companies and stuff do that, maybe yearly or whatever their situation is. That's not always as good as hands on or taking an actual class." (P6)
	Marketing strategies	11	"…one of our stores did little bag stuffers for patients that were on opioids...I don't know if we did a Facebook campaign or not. I can't remember all of the advertising. None of it was really successful, and I think we really backed off of it. But it wasn't advertising on TV or radio." (P1) "…maybe even like just a flier or something, just so people know that there is something out there…maybe they don't know that naloxone even exists and what it can do." (P4) "Most of my patients I know how much their dosage is, but bag stuffers would help." (P5)

			"As far as the sticker…I have a little paper sheet that says OCC on it for opioid counseling." (P10)
	Finding more affordable options for patients (naloxone kits, manufacturer coupons)	5	"…we [the pharmacists] wanted to offer a more affordable alternative to Evzio and even Narcan. We just did our own research and decided the naloxone injection and it can be drawn up from vials, probably a little bit more affordable than Narcan or Evzio." (P2) "We try to offer a more affordable one with two syringes and two vials of the naloxone…and we were…more successful at dispensing that than we were the Narcan nasal spray." (P1) "…insurance would pay and then the company, Kaleo…they would put on a manufacturer coupon electronically…They had to pay $30.00 co-pay [for Evzio]" (P6)
	Readily available resources for patients	5	"I think one huge area that's missing as far on the abuse side is we've identified these people who are abusers, but now what do we do?…I wish there was just some way we could get them into some emergent three day program that would buy them time until they could get into a rehab, or get into an outpatient program or something. That would be great." (P5) "…the [naloxone] package itself…[came with] a printout with pictures and images. I had that printout where I gave them [the caregiver] what to look for and what to do. What process they should go through. It was pretty quick." (P10)
	Establishing a leader/champion	2	"You also have to have leadership skills. Somebody has to be the advocate for it [naloxone services], whether it's your company, whether it's the pharmacist in charge at a location, or the district manager." (P6)
	Ensuring an appropriate physical setting (consultation room, etc)	1	"I might just do it [counsel about opioids and naloxone] at the counter with the registers, but if there's other people there I tell them let's go over to this corner where we have a little cubicle almost" (P10)
FACILITATOR: EXTERNAL ENVIRONMENT (n=18)	Advocating for national or state-wide policy changes	15	"Or even making it [naloxone] part of like a REMs program to make sure that they're counseled on it." (P4) "…insurances…the protocol for how that works for the billing. They could get on board with the [naloxone] policy and maybe not make it so expensive for the patients." (P4)

137

			"I think one thing that would help honestly is if you got a pain prescription over so many morphine equivalents you had to get a Narcan once a year. Or you had to get a form of a Naloxone once a year. And it would help too with insurance companies if they would do one Narcan nasal spray once a year for free. Honestly, for them that wouldn't be such a huge cost to absorb and it would save lives." (P5) "…talking about a statewide thing…make it a live CE that the Board of Pharmacy could require for everybody…That would be nice if they had some collaboration with some independents, and chain retailers, and mass merchandisers…to require three hours of CE…throughout the state...Make it as accessible and as easy as possible." (P6)
	Promoting local and community partnerships (health fairs, local law enforcement, etc)	3	"…getting the word out to the community that there are things that can help in the event of an overdose...Like ask your doctor about it or ask your pharmacist about it." (P4) "…we had this one physician who would write really huge quantities [of opioids]. We got really involved with the local police department here, and so the narcotics' agent there has gone to work for the DEA. We…see him every three, four or five years when we have a DEA conference…They just kind of tell us, off the record what's going on." (P7)

[a]n=frequency with which the theme/category was coded across transcripts

4.1.2.2 Current Implementation Strategies

When asked about their current pharmacy-based naloxone services implementation strategies, pharmacists discussed 17 themes (Table 4.10) across 3 categories: workflow (8 themes); marketing (4 themes); and communication (5 themes).

Workflow

Eight themes were identified related to naloxone workflow strategies currently implemented in community pharmacies in Alabama (Table 4.10). The most commonly cited theme was integration into the prescription dispensing workflow (n=21), followed by the wait-and-see approach (n=18), and utilization of pharmacy technicians or students (n=17). In terms of integrating naloxone provision into the prescription workflow, pharmacists discussed company policies and protocols being used to encourage naloxone services as well as the use of reminder aids like stickers in prescription bags to alert the pharmacist to opioid/naloxone counseling opportunities. The wait-and-see approach was a method of interacting with patients that described pharmacists providing naloxone or discussing naloxone with patients only after receiving a physician's prescription or after being asked by the patient. This wait-and-see approach to interacting with patients (n=18) was mentioned more frequently than the proactive approach (n=7), which involved pharmacists actively seeking out opportunities to discuss or provide naloxone to patients, in which the pharmacist initiated the conversation or process. For the use of pharmacy technicians, their role in alerting pharmacists to opioid/naloxone counseling opportunities was mentioned.

Using a targeted approach (n=11), centralization (n=6), and a universal approach (n=4) were discussed less frequently. In terms of the targeted approach, this encompassed pharmacists

identifying patients to whom they could recommend naloxone based on specific high-risk opioid medications, high opioid doses, or multiple high-risk medications. Pharmacists discussed using the targeted approach more often than the universal approach to identify patients to whom they could recommend naloxone. The universal approach to identification involved recommending naloxone to all patients prescribed an opioid, regardless of type or dose. Regarding centralization, this theme refers to identification of patients potentially in need of opioid/naloxone counseling at the corporate level (or from a call center). The least commonly discussed theme was follow-up with patients (n=1), with one pharmacist describing a phone-call system to follow up with patients after dispensing naloxone.

Marketing

Four themes were identified related to naloxone marketing strategies currently implemented in community pharmacies in Alabama (Table 4.10). The most commonly discussed theme was in-store advertisements, bag stuffers, and flyers (n=5). This is exemplified by one pharmacist saying, *"...one of our stores did little bag stuffers for patients that were on opioids."* Personal selling (n=4) and community outreach (n=3) were the next most common, with pharmacists discussing face-to-face conversations with patients and mini "health fairs" or "ask the pharmacist" days in the pharmacy for patients/caregivers to come in and ask questions and be educated about opioids/naloxone. Social media campaigns (n=1) were least frequent.

Communication

Five themes were identified related to naloxone communication strategies currently implemented in community pharmacies in Alabama (Table 4.10). The most commonly cited theme was emphasizing the desire to ensure the patients' safety (n=24). In regards to this theme,

pharmacists mentioned using safety-centered language, with one pharmacist stating, *"It's kind of back to the Epi-pen thing. You say this [naloxone] is simply for emergency."* Using elements of motivational interviewing or MI (n=12) was the next most frequently discussed theme, followed by involving the whole family in the conversation (n=10). In terms of motivational interviewing, pharmacists mentioned using sensitive language and asking patients' permission to discuss naloxone. Further, one pharmacist stated, *"we will…talk to them about…how to use the naloxone, and to make sure that the people in that family are aware of how to use it."* Pharmacists also mentioned building trust by using a straightforward approach (n=9), and lastly appealing to the patients' desire to keep others around them safe "just in case" (n=8). One pharmacist mentioned that being honest and straightforward in their conversations helped them to build a team-like atmosphere with their patients and physicians, while another stated that *"when you bring it up, the point of it being accidental overdose, like… 'what if your child took your medicine…?' That makes people more receptive."*

Table 4.10. Naloxone Service Implementation Strategies Practiced by Alabama Community Pharmacists (10 Pharmacists)

Categories	Themes	n[a]	Representative Quote
WORKFLOW STRATEGIES (n=85)	Integrate into prescription workflow	21	"It's just a part of our daily dispensing habits now and I see people come in wanting oxycodone or hydrocodone." (P1) "…if you work that [naloxone provision] into a good workflow, it makes it a little easier. Our company has it pretty well where if you have special or certain drugs, certain opiates, and it's a certain dosage, you should offer [naloxone]. Just make the offer…You're not liable for anything…" (P6) "As far as the sticker [in prescription bags]…I have a little paper sheet on it that says OCC on it for opioid counseling." (P10)
	Wait-and-see approach	18	"We do dispense it [naloxone] quite a bit, but as far as us dealing with that prescription we do not. I don't know what the law is for, but I know we don't dispense it without a prescription. We only dispense it with a prescription." (P2) "…most of the conversations [about naloxone] were started by the patient." (P1)
	Utilizing pharmacy technicians or students	17	"I have one tech who's pretty trained…she knows how to use it [naloxone]. She knows when it's appropriate and stuff, and she kind of knows more which patients would need it." (P5) "…we have one technician that's amazing, that is so educated…She's very aware of naloxone, how to use it, the patients that we should actually counsel on it. She was even for it. She'll call you [when] it's time that we need to get [counsel] this one [patient]." (P2)
	Targeted approach	11	"We do have some stances as far as everything is individualized….It's simply everybody is individualized and the number one thing is just communication." (P6) "If I've seen the prescription [opioid] exceeded whatever the predetermined limit is then I could write the naloxone fill with that prescription. That would make it easier than anything." (P7)

	Proactive approach	7	"We also have that standing order for the Narcan dispensing that we keep just in case anyone does want it. We've let them know that we do offer it in case it is something they want to have on hand." (P10) "When someone comes in with a control and we look at the prescription, if this is a really high doses of controlled or multiple controlled prescriptions, then we'll talk to them, me and my partner both, we will either talk to them about the possibility of getting a prescription for the naloxone, and how to use the naloxone." (P2)
	Centralization	6	"…we started doing the opioid counseling that pops up in one of our central locations…patients who have been taking it [opioids] for years" (P10) "Actually we have [a] list printed out…We have in our main office someone who actually takes care of all our MTM…She's the one who gave me that list…for opioid counseling" (P10)
	Universal approach	4	"…if someone accidentally takes too much [opioid], maybe not the patient, it's [naloxone] there and you can rescue them. If that's the goal, then it should be dispensed with every single prescription. (P9) "I'm not saying it [naloxone] should be super-cheap and easy, but if you're going to have it out there then it should just go with every single prescription [opioid] every single time because if you say, 'Oh, they have to have a naloxone prescription at least once a year,' it's just going to fall through the cracks." (P9)
	Follow-up with patients	1	"And usually…this [naloxone] goes through what we call our specialty program, so we have a system where we do a follow up phone call. Or if the patient picks it up we'll do it in person and we'll go through a list of questions about do they know when to administer it, do they know how to administer it, did they have a family member or roommate or somebody that they can also talk to about how to administer it." (P5)
MARKETING STRATEGIES (n=13)	In-store advertisements, bag stuffers, flyers	5	"I think one of our stores did little bag stuffers for patients that were on opioids." (P1) "…just a flier…just so people know that there is something out there…maybe they don't know that naloxone even exists and what it can do." (P4)

	Personal selling	4	"I've told them, 'It's something we'll always have available for you…anytime you need it, you just let me know.'" (P10) "I think honestly just a face to face conversation would help." (P5)
	Community outreach	3	"…getting the word out to the community that there are things that can help in the event of an overdose." (P4) "…education… 'Come in, sit down with your pharmacist, we'll go over your medication with you or your family members'…it would make the people more comfortable that they're not just being targeted. That they can willingly come in and ask questions." (P10)
	Social media campaigns	1	"…we did a Facebook campaign…" (P1)
COMMUNICATION STRATEGIES (n=63)	Emphasize desire to ensure patients' safety	24	"…they're probably open to understanding this is for emergencies…It's kind of back to the Epi-pen thing. You say this [naloxone] is simply for emergency. We're not trying to…insinuate 'you definitely need this because I'm sure you're taking too many.'" (P6) "I think we just need to show…them that it's not a trust issue, that we don't trust them to take their medication properly, it's just…at any point there could be a change in the way their body reacts to these drugs [opioids]…when people get older, their breathing patterns change…subtle changes can actually make the dose a lot more potent…and then side effects do occur." (P8)
	Use elements of MI (ask permission, assess readiness, roll with resistance, sensitive language)	12	"…as clearly and peacefully as possible with a calm demeanor and everything. I'll just…talk it through." (P5) If you look at someone and you can tell maybe they're a little open to listening to you…talk to the patient first…get their permission and say 'would you like me to do that?' To a big extent, if they feel like you're on their side, sometimes they are more willing to say okay." (P6)
	Involve the whole family in the conversation	10	"…we will…talk to them about…how to use the naloxone, and to make sure that the people in that family are aware of how to use it." (P2) "You have a lot of family members that pick up. You would have to explain it [naloxone]." (P3)

144

	Build trust by using a straightforward approach	9	"…if you're honest with people or you're honest with the physicians and you're honest with patients, then we have a team-building thing where we can maybe actually help people." (P9) "To some extent laying out there is an issue. 'It's a serious problem' and being honest." (P6)
	Appeal to patients' desire to keep others around them safe "just in case"	8	"I kinda took the approach with them, you know, just keep this around. It could save your life, or if someone got into your supply, you could save their life in the event of an overdose… like your grandkids or your kids got into it" (P4) "…when you bring it up, the point of it being accidental overdose, like… 'what if your child took your medicine, or your grandmother took your medicine?' That makes people more receptive." (P5)

MI=Motivational interviewing

[a]n=frequency with which the theme/category was coded across transcripts

4.1.3 Expert Interviews

A maximal variety of 6 experts were interviewed (see Tables 4.2a and 4.2b) in order to compare pharmacists' current naloxone service implementation strategies to experts' recommended strategies. Expert interviews averaged 40.62 minutes in length with 243.70 minutes (4.06 hours) recorded overall for all expert interviews. An average of 5,623 words were transcribed per interview, for a total of 33,739 words overall.

Experts' interview transcripts were analyzed using a deductive method with a priori codes derived from pharmacists' current naloxone services implementation strategies presented in Table 4.10 above, with additional recommended strategies highlighted using open-coding. Experts' recommended strategies were identified across all 3 categories, including workflow (8 strategies), marketing (5 strategies), and communication (5 strategies), and are elaborated upon below (Section 4.1.3.1, Tables 4.11-12).

Table 4.11 Categories Deductively Identified from Expert Interviews

No.	Category	# Strategies
	Recommended Naloxone Service Implementation Strategies	**17**
1	Workflow	8
2	Marketing	5
3	Communication	5

4.1.3.1 Recommended Implementation Strategies

When asked about best practices and strategies to enhance naloxone services implementation in community pharmacies, experts recommended strategies that were categorized as workflow, marketing, or communication-related. Overall, 8 workflow strategies were recommended by experts (Table 4.12). The most frequently recommended strategy was using universal approach to identify patients who benefit from naloxone (n=28), followed by

using a proactive approach to interact with patients (n=23) and integrating naloxone services into the prescription dispensing workflow (n=22). Follow-up with prescribers after providing naloxone (n=17) and using a targeted approach to identify patients (n=14) were discussed with moderate frequency, followed by utilizing pharmacy technicians or students (n=7) and two-way referral of patients between the pharmacy and treatment centers and vice versa (n=7). Follow-up with patients was also recommended (n=3), but less frequently. Experts did not discuss centralization or using a wait-and-see approach.

Next, 5 marketing strategies were recommended. Experts most frequently recommended using personal selling (n=16) to enhance uptake of community pharmacy-based naloxone services by patients and prescribers. Use of in-store advertisements, bag stuffers, and flyers (m=7) and community outreach (n=5) were recommended with moderate frequency. Experts also discussed using TV, radio, and print advertisements (n=2) as well as social media campaigns (n=1), but mentioned that these strategies may be more or less feasible depending on particular pharmacy organizations' regulations and policies. For example, these last 2 strategies may be initiated at the corporate level (rather than individual pharmacist level) in some organizations.

Last, 5 communication strategies were recommended. The most frequently recommended strategies were using elements of MI (n=30) and emphasizing the desire to ensure patients' safety (n=27). Appealing to patients' desire to keep others around them safe (n=15), building trust by using a straightforward approach (n=14), and involving the whole family in the conversation (n=13) were discussed with moderate frequency.

Table 4.12 Naloxone Service Implementation Strategies Recommended by Experts (6 Experts)

Categories	Themes	n[a]	Representative Quote
WORKFLOW STRATEGIES (n=121)	Universal approach	28	"…what I lecture about all the time is that it [offering naloxone] should be universal…don't make it optional because the moment that you have to think about, 'Is this [the type of] person who most often…?' you're going to feel like you're selecting someone out. You feel like you're stereotyping." (E6) "If it's in a busy chain setting where they've waited in line for thirty minutes…and the pharmacist says, 'You've been flagged as potentially at risk of opioid overdose. We recommend that you have this Narcan.'…I don't think that's going to go very well." (E5) "…we recommend offering naloxone with every opioid prescription…because the more we push for naloxone for everyone, hopefully we'll move a little bit in that direction." (E5) "It's going to be very difficult for pharmacists to assess the entire picture because pharmacists are really, really busy at a community pharmacy setting, so the easiest thing is whenever they see opioid prescriptions, and then they can just think about, 'Okay, probably this patient needs to have Naloxone.'…they can automatically dispense Naloxone." (E2)
	Proactive approach	23	"I think with naloxone, it should not be an offer. It should be 'you're not getting this drug [prescription opioid] until we have a chat.'" (E2) "…until pharmacists start making [naloxone] recommendations and say, 'Well this is no big deal.' …Once you do one, or two, or three, or five, the next 500 aren't that big a deal. I think when we get experience talking to high and low risk groups then it becomes just standard and becomes not a big deal." (E6)
	Integrate into prescription workflow	22	"Making sure that there's a patient handout that goes with it [naloxone]…you don't want to be pulling out the package insert trying to work through it with the patient. Making sure that you're prepared to provide that type of counseling if the person says, 'Yes, let's do it.'" (E3) "…any demographic that gets integrated into our daily patient flow becomes de-stigmatized…I think that we need to take that model and to say, 'co-

			prescribing naloxone is just an essential part of opioid dispensing,' or 'A naloxone going out with people who buy syringes makes sense'…There's a sticker on the syringes that says, 'Buy naloxone.'" (E6) "…if there's a floater pharmacist around who doesn't normally do that [provide naloxone], they [the technician] say, "oh, this person asked for naloxone. We've got a copy of the standing order and how to write all the prescriptions over here in this drawer. Let me grab it. I can enter it, you can check it off.'' (E5)
	Follow-up with prescribers[b]	17	"I think having a feedback mechanism back to the providers…if you've got a quick fax sheet or something that says hey, FYI we did this so that they can go ahead and integrate that information onto their medical list. That might be a way to start building that relationship with medical offices." (E3) "…pharmacists can communicate with the primary care physician to suggest prescribing Naloxone, or even they can say, 'I assessed the patient's risk factors of opioid overdose, and then I prescribed the Naloxone.'" (E4) "…the medical system. I think that it's not really a thought of theirs that pharmacies are doing this [providing naloxone]. I think that they feel the same problems that pharmacies do is that they just want the loop closed. 'Did you give my patient an immunization? I need to know that,' or, 'Did you use the same order to do naloxone? I'd like to know that.'" (E6) "…many naloxone laws are written…to notify the primary care... I originally supported that because I felt that was a limitation…[for example] 20 letters saying…or 20 faxes out, 'We co-prescribed naloxone, patient was interested.'" (E6)
	Targeted approach	14	"So there are risk factors that have been identified for overdose…concomitant benzodiazepine…over 90 MME…folks in treatment especially in the first six months." (E1) "Don't let patients become widgets. Look at the patient as a whole. Don't just look at their opioid condition. Look at everything else that they're coming in for. Look at their history with you." (E2)

			"…our clinic level policy is anybody that is getting over 90 morphine equivalent doses [MMEs] per day should be prescribed naloxone. And that is clearly in our clinic policies. Our clinic policy is if somebody is between 50 and 90 [MMEs], and they have some type of other risk factor for respiratory depression, so that would be somebody who's maybe on a concurrent benzodiazepine, somebody who has some type of underlying respiratory disease or asthma, COPD, sleep apnea, those individuals should also have naloxone. Less than 50 [MMEs], our clinic doesn't have any clear guidance." (E3) "I think you have to approach it [offering naloxone] based on who you're dealing with. Is this somebody who's got cancer, do they have MS ... How old are they? …I do think you have to individualize it and you have to think about what they're using it for and approach it in a very different way for each person…" (E2)
	Utilizing pharmacy technicians or students	7	"I certainly hear from my pharmacy students that after receiving training, they have educated their pharmacists, corrected inaccurate understandings, lack of knowledge among their pharmacists. And they have even initiated conversations or responded to conversations with patients about naloxone." (E5) "…when an electronic prescription comes in or somebody drops off a prescription…at drop off the technician can say, "We'd like you to talk to the pharmacist about naloxone to keep you and your family safe." It tends to be scripts." (E6)
	Two-way referral[b]	7	"…as a profession we start thinking about what are those frameworks to better ensure communication between the community setting to medical office setting and then vice versa…I think the more that you can build relationships between medical offices and community pharmacies about communication preferences, about those things that they want, I think that that's how you're going to get physician offices to want to engage more with the community pharmacies." (E3) "I certainly could see developing that sort of relationship for referrals [from physician offices] and maybe especially an independent pharmacy might be a potential financial benefit to saying, 'when you're worried about a patient, or

150

			even if you're just prescribing opioids for chronic pain, if you send them to me and encourage them to have all their prescriptions filled with me, I'll review their charts and I'll determine which patients are at risk and get them naloxone. I care about that, I will help you keep your patients safe.'" (E5) "For people who might come in and request naloxone and who you suspect might be using illicit substances, a referral to a local Harm Reduction Coalition might be appropriate, and many of them distribute naloxone for free. At the Harm Reduction Coalition website…they actually have a tool to search for local Harm Reduction Coalitions, needle exchanges, and naloxone distribution programs." (E5)
	Follow-up with patients	3	"…if someone's asking for it [naloxone] or it's co-prescribed, this is your once a year opportunity to assess what's going on in that person's life." (E6) "Check back in with patients. Try to keep track of how things are going. Positive feedback is extremely helpful…As a pharmacist you don't usually get to save a life, or you don't know…I think that creates a positive feedback loop where you feel passionate about recommending it [naloxone], more comfortable doing so because you see that there are positive outcomes." (E5)
MARKETING STRATEGIES (n=31)	Personal selling	16	"…if the patient received any education regarding opioid overdose at a clinic, but people tend to forget. That's why if pharmacists can emphasize the importance of knowing what opioid overdose is, and then emphasize the importance of naloxone, the patient is able to receive education at least twice." (E4) "…academic detailing…is probably some of the most effective and underutilized efforts that can be done by pharmacy students and RA's…having a conversation, practicing a conversation." (E6) "…you could create a relationship where a local physician knew, 'hey, if you send people to my pharmacy specifically,' especially with an independent pharmacy, if you call around and you say, 'hey, when you have patients who you think might be at risk for overdose, send them to me and I will educate them about naloxone. I will help them pick the right formulation so you don't have to spend that time.'" (E5)

			"…a physician might be more likely to be on board with that [pharmacy-based naloxone provision] if you were offering a more comprehensive set of services. I have heard of a few instances of pharmacists who are administering, for example, extended release naltrexone on a monthly basis. So that might be another service you could provide to break into offering more addiction-oriented care out of the pharmacy." (E5)
	In-store advertisements, bag stuffers, flyers	7	"…put little tags on the bags for opioid prescriptions that require naloxone." (E6) "From a really practical standpoint, I think just putting up a sign in the pharmacy, almost like a banner that shows that they have flu shots, putting up a sign that says, "We want to keep you safe. We have naloxone; ask the pharmacist," I think that could help because then it makes it seem like it's normal." (E5)
	Community outreach	5	"…figuring out how to best meet the needs of their community. Every community can be different. I live in primarily a geriatric community, that education need is gonna be a little different than if you're in more of an urban setting like Jefferson County…So each pharmacist would have to determine what the education need is and then in my community I would never really try to do it with a video, whereas that might work better in some other communities." (E1) "I would say personally that direct outreach has a greater potential for benefit…" (E5)
	TV, radio, print advertisements[b]	2	"…a large campaign with billboards on the freeway." (E4)
	Social media campaigns	1	"They [pharmacists] may be limited by their employer, or they may be promoted by their employers. [A corporately-owned pharmacy] just went nationwide with public services announcements and posts." (E6)
COMMUNICATION STRATEGIES (n=99)	Use elements of MI (ask permission, assess readiness, roll with resistance, sensitive language, cultural competency)	30	"It takes either a longer conversation than I think most pharmacies have in the community setting or requires circling back to this conversation where you have kind of implanted those seeds. Somebody maybe has ruminated on this a little bit and you're coming back and you can kind of re-expand onto that conversation." (E3) "Using sensitive language, patient centered language." (E6)

	Emphasize desire to ensure patients' safety	27	"…with fentanyl, which we regularly use with our hospice patients, it really doesn't take very long for somebody to succumb. It can be within a couple minutes. EMS response times are not that fast. If you compare that to having naloxone on hand to me there's not a question." (E1) "Based on my experience, sometimes the patient is against having naloxone, this is because the patient thought we the healthcare provider misunderstood the patient, so when we open the discussion regarding opioid overdose, sometimes patients say, "Why are you saying I am at risk of opioid overdose?" Or, "Are you saying I am abusing opioids?"…But after that I said, "You know what? We don't think you are abusing the medications, we are concerned about your health," and then the patient changes their attitude a lot, and then they would accept having naloxone available." (E4) "It's [naloxone] the same as having a fire extinguisher or an EPI-pen." (E6)
	Appeal to patients' desire to keep others around them safe "just in case"	15	"…there's always a risk in hospice, there's young children in the home, we're dispensing large quantities of opioids in hospice settings. And so we actually encourage hospice families to keep naloxone in the home…Sometimes when people are going through the dying process there's times of chaos, you just never know." (E1) "People are coming in with their children, if they're coming with their family members, if they're coming in with a companion animal, it's not just that patient that's at risk for respiratory depression [from opioids]. It's usage by other people that might be important to them." (E3)
	Build trust by using a straightforward approach	14	"I think it's better for pharmacists to discuss with the patient about whether patient has naloxone, whenever they see opioid prescriptions, so that the patient is aware that naloxone is important for opioid overdose prevention." (E4) "People [patients] didn't like things like [the pharmacist saying], 'The CDC says that now government's involved [in opioid dispensing],'…you're talking about the pharmacist-patient relationship." (E6) "I think if you have an open conversation with someone who has a history of opioid use disorder or illicit opioid use in their chart about naloxone, I've

153

| | | | never had really any pushback on that. So I think pharmacists just have less comfort talking to those patients, and in a community setting you almost never know that somebody's doing that because they're so unlikely to tell you. So I do think the key for chronic opioid patients, prescription opioid patients, is to approach it in a non-stigmatizing manner and let them know you're not judging them, and I think for illicit opioid use in a community setting, it's just not hassling people, not asking them a bunch of questions if they request naloxone. Just give it to them and teach them how to use it…" (E5) |
| | Involve the whole family in the conversation | 13 | "One of the things I think is it's important if somebody's going to either buy naloxone or fill a prescription for naloxone one of the biggest mistakes I've seen is whether you educate them personally or you have them watch a video, however you're going to educate them, is that the education is not given to everybody in the home." (E1)

 "Sometimes you have people who have families that are supportive, and unfortunately sometimes you don't…there's a familial cultural role in a lot of this. But if there are families or caregivers or something along those lines that are near them [the patient], we can always make the offer to them." (E2) |

MI=Motivational interviewing

[a]n=frequency with which the theme/category was coded across transcripts

[b]Strategies recommended by experts that were not practiced by interviewed pharmacists

Additionally, based on the recommended naloxone service implementation strategies above, and taking into account the recommended strategies that were not currently being implemented by pharmacists, a secondary analysis was performed to identify experts' recommended priority areas for action. In other words, we wanted to explore whether there was a larger pattern or meaning behind experts' recommended strategies across the workflow, marketing, and communication domains. What were the common threads throughout these recommended strategies? To achieve this, deductively-identified strategies presented above (Table 4.12) were treated as a priori codes and re-grouped by LAH into alternative broad units of meaning (Round 1), from which initial categories were inductively identified and named. Some strategies/codes were kept while others were excluded to create final categories (Round 2). Final categories were then consolidated to form one overarching "big picture" theme related to experts' recommendations to enhance naloxone services implementation (Round 3) (Table 4.13).

Table 4.13 Secondary Analysis of Expert Interviews: Mixed Deductive and Inductive Process

Round	Actions
1	Experts' recommended workflow, marketing, and communication strategies were treated as a priori deductively-identified codes and inductively grouped into initial broad categories based on "big picture" meaning.
2	Some strategies/codes were kept and some were excluded to create final categories.
3	Final categories were consolidated to create on overarching "big picture" theme regarding experts' recommendations to enhance pharmacy-based naloxone services.

The overarching theme that was identified was, "Creating a Normative Culture of Safety in the Pharmacy." As mentioned above, this was based on larger units of meaning inductively derived from experts' recommended workflow, marketing, and communication strategies. This overarching theme and underlying categories are elaborated upon in the following section.

4.1.3.2 Creating a Normative Culture of Safety

The overarching theme identified from experts' recommended strategies (see Table 4.12 for strategies) was enhancing community pharmacy-based naloxone services implementation by creating a normative culture of safety in the pharmacy. This overarching theme was based upon 3 specific sub-themes or categories (Table 4.14) related to priority areas for action into which strategies were inductively grouped, namely: 1) using safety-centered marketing materials and communication strategies (n=95); 2) using a universal approach versus targeted approach (n=42); and 3) closing the loop (n=27).

Table 4.14 Priority Areas for Action Identified from Expert Interviews

No.	Themes and Categories	# Strategies
	Creating a Normative Culture of Safety	**10**
1	Using Safety-Centered Marketing Materials and Communication Strategies	5
2	Using a Universal Approach versus Targeted Approach	2
3	Closing the Loop	3

Each of these categories, or priority areas for action, is explained in more detail below (Table 4.15).

Priority Area 1: Using Safety-Centered Marketing Materials and Communication Strategies

The first priority area for action to create a normative culture of safety in the pharmacy was using safety-centered language in marketing materials and during pharmacist-patient communication (n=95; Table 4.15). This could be accomplished through personal selling (n=16) or in-store advertisements like bag stuffers, flyers, or intercom announcements (n=7). Furthermore, a culture of safety is created by using sensitive language and other elements of MI (n=30), emphasizing the pharmacists' desire to ensure patients' safety (n=27), and appealing to patients' desire to keep others around them safe (n=15). Experts emphasized that by creating a

culture of safety rather than a culture of suspicion, these strategies help to decrease patient resistance to receiving naloxone.

Priority Area 2: Using a Universal Approach versus Targeted Approach

The second priority area for action to create a normative culture of safety in the pharmacy was using a universal approach versus targeted approach to identify patients who may benefit from naloxone (n=42; Table 4.15). In addition to more frequently recommending the universal approach (n=28) than the targeted approach (n=14), experts discussed that using a universal approach decreases missed opportunities and reduces patients' perception of "stereotyping" compared to the targeted approach. They also mentioned that while the targeted approach may be more cost-effective in terms of providing naloxone only to those at highest risk, this approach may be inefficient and too time-consuming in the busy community pharmacy setting.

Priority Area 3: Closing the Loop

The third priority area for action to create a normative culture of safety in the pharmacy was "closing the loop" (n=27) by following up with prescribers (n=17) and patients (n=3) after naloxone is dispensed (Table 4.15). Experts further recommended that in addition to following up after dispensing naloxone, pharmacists can enhance naloxone services implementation and foster a culture of safety by establishing two-way referral networks whereby: 1) pharmacists refer patients at risk of opioid overdose to appropriate treatment centers or prescribers if specialized care is needed; and 2) prescribers refer patients on chronic opioid prescriptions or otherwise at risk of opioid overdose to the pharmacy to receive naloxone. Experts mentioned that doing so creates a trusting relationship and network of care between the patient, prescriber, and pharmacy.

Table 4.15 Priority Areas for Action to Create a Normative Culture of Safety in the Pharmacy and Enhance Naloxone Services Implementation

Priority Area for Action	Strategy / Support for Priority Area	n[a]	Representative Quote
Using Safety-Centered Marketing and Communication Strategies (n=95)	Personal selling	16	"…academic detailing…is probably some of the most effective and underutilized efforts that can be done by pharmacy students and RA's…having a conversation, practicing a conversation." (E6) "…you could create a relationship where a local physician knew, 'hey, if you send people to my pharmacy specifically,' especially with an independent pharmacy, if you call around and you say, 'hey, when you have patients who you think might be at risk for overdose, send them to me and I will educate them about naloxone. I will help them pick the right formulation so you don't have to spend that time.'" (E5)
	In-store advertisements, bag stuffers, flyers	7	"From a really practical standpoint, I think just putting up a sign in the pharmacy, almost like a banner that shows that they have flu shots, putting up a sign that says, 'We want to keep you safe. We have naloxone; ask the pharmacist,' I think that could help because then it makes it seem like it's normal." (E5)
	Use elements of MI (ask permission, assess readiness, roll with resistance, sensitive language, cultural competency)	30	"Using sensitive language, patient centered language." (E6)
	Emphasize desire to ensure patients' safety	27	"It's [naloxone] the same as having a fire extinguisher or an EPI-pen." (E6)
	Appeal to patients' desire to keep others around them safe "just in case"	15	"People are coming in with their children, if they're coming with their family members, if they're coming in with a companion animal, it's not just that patient that's at risk for respiratory depression [from opioids]. It's usage by other people that might be important to them." (E3)
Using a Universal Approach versus Targeted Approach (n=42)	Universal Approach	28	"…what I lecture about all the time is that it [offering naloxone] should be universal…don't make it optional because the moment that you have to think about, 'Is this [the type of] person who most often…?' you're going to feel like you're selecting someone out. You feel like you're stereotyping." (E6)
	Targeted Approach	14	"…our clinic level policy is anybody that is getting over 90 morphine equivalent doses [MMEs] per day should be prescribed naloxone. And that is clearly in our clinic policies. Our clinic policy is if somebody is between

			50 and 90 [MMEs], and they have some type of other risk factor for respiratory depression, so that would be somebody who's maybe on a concurrent benzodiazepine, somebody who has some type of underlying respiratory disease or asthma, COPD, sleep apnea, those individuals should also have naloxone. Less than 50 [MMEs], our clinic doesn't have any clear guidance." (E3)
Closing the Loop (n=27)	Follow-up with prescribers	17	"I think having a feedback mechanism back to the providers…if you've got a quick fax sheet or something that says hey, FYI we did this so that they can go ahead and integrate that information onto their medical list. That might be a way to start building that relationship with medical offices." (E3)
	Two-way referral	7	"…as a profession we start thinking about what are those frameworks to better ensure communication between the community setting to medical office setting and then vice versa…I think the more that you can build relationships between medical offices and community pharmacies about communication preferences, about those things that they want, I think that that's how you're going to get physician offices to want to engage more with the community pharmacies." (E3)
	Follow-up with patients	3	"Check back in with patients. Try to keep track of how things are going. Positive feedback is extremely helpful…As a pharmacist you don't usually get to save a life, or you don't know…I think that creates a positive feedback loop where you feel passionate about recommending it [naloxone], more comfortable doing so because you see that there are positive outcomes." (E5)

[a]n=frequency with which the theme/category was coded across transcripts

4.1.4 Comparison of Pharmacist and Expert Interviews

The alignment of pharmacists' current naloxone service implementation practices were compared to experts' recommended strategies. Detailed comparisons are below. Frequencies refer to frequency with which themes were coded across transcripts from pharmacist interviews unless otherwise noted.

4.1.4.1 Alignment of Pharmacists' Practices with Experts' Recommendations

While the majority of practices employed by community pharmacists to implement naloxone services aligned with experts' recommendations (Figure 4.2), some strategies did not align with experts' recommendations, and others were neutral (experts had no recommendation either way). Specifically, 14 practices aligned with experts' recommended strategies, 2 practices did not align, and 1 was neutral. Practices that did not align with experts' recommendations were: 1) using a wait-and-see approach (n=18); and 2) using a targeted approach (n=11). Experts were neutral with regards to pharmacists' practice of centralization or the use of a call center/central office to facilitate identification or contact of patients who may benefit from naloxone (n=6).

Furthermore, experts recommended 3 strategies that were not currently being practiced by pharmacists: 1) follow-up with prescribers (n=17 expert recommendations); 2) two-way referral (n=7 expert recommendations); and 3) TV, radio, and print advertisements (n=2 expert recommendations).
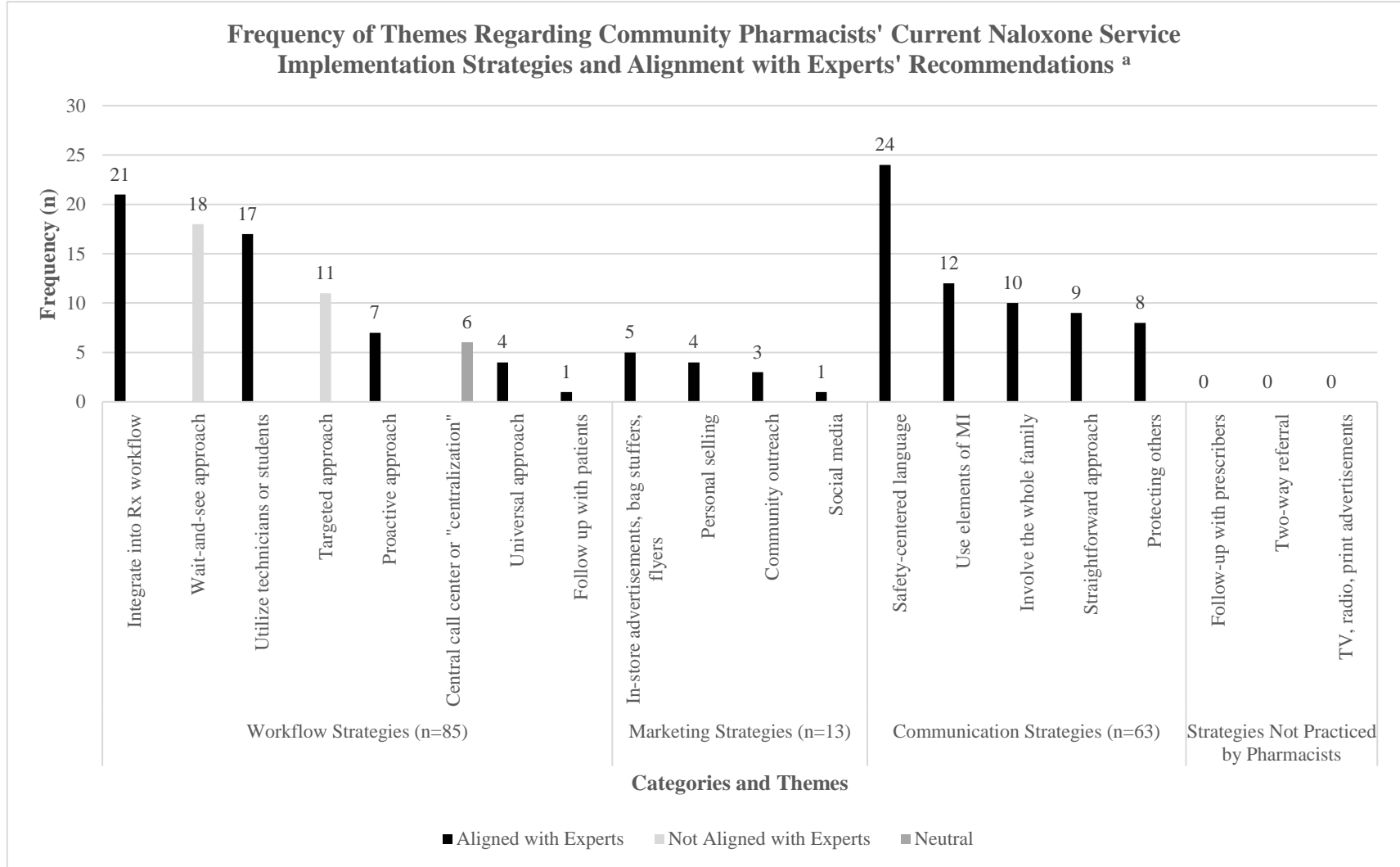
Figure 4.2 Frequency of Themes Regarding Community Pharmacists' Current Naloxone Service Implementation Strategies and Alignment with Experts' Recommendations
[a]n=frequency with which the theme/category was coded across transcripts from pharmacist interviews

4.1.5 Training Program Development

4.1.5.1 Initial Training Program

The initial training program was developed by the PI (LAH) based on themes derived from the Aim 1 formative interviews (see Sections 4.1.2-4.1.4 for interview findings; see Section 4.1.6 for details of the finalized training program). Accordingly, the program was created as a live online webinar with 3 modules: 1) Naloxone Basics; 2) Implementation Strategies; and 3) Communication Strategies. Feedback from a stakeholder panel of end users and experts was then used to modify the training program's content and format to ensure optimum feasibility, acceptability, and usability of the final program. Parallel questions were used to assess the feasibility, acceptability, and usability of each module. The results of this feedback process are presented below (Section 4.1.5.2).

4.1.5.2 Stakeholder Panel Feedback

A stakeholder panel was recruited by email using Aim 1 interview participants as an initial sampling frame. Panelists included end users of the training program (Alabama community pharmacists) and opioid/naloxone experts. In order to recruit a sufficient number of experts with expertise in all main training needs identified from formative interviews (Modules 1-3), the sampling frame was expanded to include content experts from additional university and clinical practice sites in Alabama. A total of 10 stakeholder panelists were recruited (Table 4.16), including 3 Alabama community pharmacists and 7 experts (3 opioid/naloxone experts and 4 specialized content experts).

Table 4.16 Stakeholder Panel Participant Characteristics (N=10)

Codename	Age (Years)	Sex	Race	Job Title	Pharmacy Type	Pharmacy Location	Modules Assessed
Alabama Community Pharmacists (n=3)							
P2	55	Female	Black	Staff pharmacist	Corporately-owned	Urban	1-3
P4	30	Female	White	Pharmacist-in-charge	Independently-owned	Urban	1-3
P6	37	Male	White	Pharmacist-in-charge	Corporately-owned	Urban	1-3

Codename	Age (Years)	Sex	Race	Main Practice Site(s)	Practice Location	Expertise	Modules Assessed
Opioid/Naloxone Experts (n=3)							
E3	35	Female	White	• Ambulatory Care	Oregon	• Clinical	1-3
E4	45	Female	Asian	• Academia	New Mexico	• Pedagogical	1-3
E5	29	Male	White	• Academia • Ambulatory Care • Public Health	Texas	• Clinical • Pedagogical	1-3
Specialized Content Experts (n=4)							
E2 [a]	34	Female	White	• Hospital or Acute Care	Alabama	• Naloxone pharmacology • Emergency services	1
E7 [a]	NR	Female	White	• Academia • Ambulatory Care	Alabama	• Naloxone service implementation	2
E8 [a]	NR	Male	White	• Academia • Ambulatory Care	Alabama	• Psychology • Communication • Substance use disorder	3
E9	NR	Male	White	• Academia • Ambulatory Care	Alabama	• Psychology • Communication • Substance use disorder	3

[a] Served as an expert speaker for delivery of the training program in Aim 2

NR = no response or unknown

The initial training program was then provided electronically to the stakeholder panel and their feedback was obtained across 2 rounds of iterative feedback and modification via: 1) self-administered online questionnaire among community pharmacists and opioid/naloxone experts (Round 1); and 2) in-person, email, and/or videoconference (depending on their availability) with fieldnotes among specialized content experts (Round 2). See Table 4.17 for details regarding actions taken in Rounds 1-2. The training program was finalized after the second round of feedback.

Table 4.17 Actions Taken During Rounds 1 and 2 of Stakeholder Panel Feedback

Round	Feedback Mode	Actions	Panelists (n)
1	Self-administered online questionnaire	Feedback on initial (version 1) training program content and format. Modification of training materials based on feedback to create version 2 of the program.	Community pharmacists (3) Opioid/naloxone experts (3)
2	In-person, email, and/or videoconference with fieldnotes	Feedback on training program v2 content and format. Further modification of training materials based on feedback to create the finalized (version 3) program.	Specialized content experts (4)

For Round 1, a total of 6 stakeholder panelists (n=3 community pharmacists and n=3 opioid/naloxone experts) were asked to complete the self-administered online training program feedback form (Table 4.17; see Appendix B for the detailed questionnaire). Respondents' ratings of the feasibility, acceptability, and usability of the training program content and format for Modules 1-3 are presented in Tables 4.18a-c below. Overall, the feedback was generally positive.

For Module 1, the majority (66.7%) of panelists strongly agreed that they were satisfied with the information presented in the module overall, while 66.7% strongly agreed that the overall appearance of the module was pleasing to the eye. Furthermore, 66.7% strongly agreed

that the information presented in Module 1 was useful for practicing Alabama community pharmacists.

For Module 2, 50.0% of panelists strongly agreed that they were satisfied with the information presented in the module overall, while 66.7% strongly agreed that the overall appearance of the module was pleasing to the eye. Furthermore, 50.0% strongly agreed that the information presented in Module 2 was useful for practicing Alabama community pharmacists.

For Module 3, 50.0% of panelists strongly agreed that they were satisfied with the information presented in the module overall, while 50.0% strongly agreed that the overall appearance of the module was pleasing to the eye. Furthermore, 50.0% strongly agreed that the information presented in Module 3 was useful for practicing Alabama community pharmacists.

Table 4.18a Round 1 Feedback: Frequency of Panelists' Ratings Regarding Training Program Feasibility, Acceptability, and Usability in Module 1

Module 1	All (N=6) n (%)	Community Pharmacists (N=3) n (%)	Experts (N=3) n (%)
Feasibility, mean (SD)	4.67 (0.52)	5.00 (0)	4.33 (0.58)
The information presented in Module 1 was useful for practicing Alabama community pharmacists			
Strongly disagree	-	-	-
Disagree	-	-	-
Neither agree nor disagree	-	-	-
Agree	2 (33.3)	-	2 (66.7)
Strongly agree	4 (66.7)	3 (100.0)	1 (33.3)
Acceptability, mean (SD)	4.50 (0.80)	5.00 (0)	4.00 (0.92)
I was satisfied with the information presented about the current opioid landscape			
Strongly disagree	-	-	-
Disagree	-	-	-
Neither agree nor disagree	1 (16.7)	-	1 (33.3)
Agree	1 (16.7)	-	1 (33.3)
Strongly agree	4 (66.7)	3 (100.0)	1 (33.3)
I was satisfied with the information presented about treatment and prevention of opioid use disorder			
Strongly disagree	-	-	-
Disagree	-	-	-
Neither agree nor disagree	2 (33.3)	-	2 (66.7)
Agree	-	-	-
Strongly agree	4 (66.7)	3 (100.0)	1 (33.3)
I was satisfied with the information presented about naloxone administration			
Strongly disagree	-	-	-
Disagree	-	-	1 (33.3)
Neither agree nor disagree	2 (33.3)	-	-
Agree	-	-	1 (33.3)
Strongly agree	4 (66.7)	3 (100.0)	1 (33.3)
I was satisfied with the information presented about naloxone dispensing laws in Alabama			
Strongly disagree	-	-	-

Disagree	-	-	-
Neither agree nor disagree	-	-	-
Agree	2 (33.3)	-	2 (66.7)
Strongly agree	4 (66.7)	3 (100.0)	1 (33.3)
I was satisfied with the information presented in Module 1 overall			
Strongly disagree	-	-	-
Disagree	-	-	-
Neither agree nor disagree	-	-	-
Agree	2 (33.3)	-	2 (66.7)
Strongly agree	4 (66.7)	3 (100.0)	1 (33.3)
Usability, mean (SD)	4.56 (0.57)	4.94 (0.10)	4.17 (0.60)
The information presented in Module 1 was accurate			
Strongly disagree	-	-	-
Disagree	-	-	-
Neither agree nor disagree	-	-	-
Agree	2 (33.3)	-	2 (66.7)
Strongly agree	4 (66.7)	3 (100.0)	1 (33.3)
The information in Module 1 was presented in sufficient detail			
Strongly disagree	-	-	-
Disagree	-	-	-
Neither agree nor disagree	-	-	-
Agree	1 (16.7)	-	1 (33.3)
Strongly agree	5 (83.3)	3 (100.0)	2 (66.7)
The text in Module 1 was easy to read			
Strongly disagree	-	-	-
Disagree	1 (16.7)	-	1 (33.3)
Neither agree nor disagree	-	-	-
Agree	2 (33.3)	-	2 (33.3)
Strongly agree	3 (50.0)	3 (100.0)	-
The text in Module 1 loaded well on my device			
Strongly disagree	-	-	-
Disagree	-	-	-
Neither agree nor disagree	-	-	-
Agree	2 (33.3)	-	2 (66.7)
Strongly agree	4 (66.7)	3 (100.0)	1 (33.3)

The graphics in Module 1 loaded well on my device			
Strongly disagree	-	-	-
Disagree	-	-	-
Neither agree nor disagree	-	-	-
Agree	3 (50.0)	1 (33.3)	2 (66.7)
Strongly agree	3 (50.0)	2 (66.7)	1 (33.3)
The overall appearance of Module 1 was pleasing to the eye			
Strongly disagree	-	-	-
Disagree	-	-	-
Neither agree nor disagree	1 (16.7)	-	1 (33.3)
Agree	1 (16.7)	-	1 (33.3)
Strongly agree	4 (66.7)	3 (100.0)	1 (33.3)

Table 4.18b Round 1 Feedback: Frequency of Panelists' Ratings Regarding Training Program Feasibility, Acceptability, and Usability in Module 2

Module 2	All (N=6) n (%)	Community Pharmacists (N=3) n (%)	Experts (N=3) n (%)
Feasibility, mean (SD)	3.83 (1.33)	5.00 (0)	2.67 (0.58)
The information presented in Module 2 was useful for practicing Alabama community pharmacists			
Strongly disagree	-	-	-
Disagree	1 (16.7)	-	1 (33.3)
Neither agree nor disagree	2 (33.3)	-	2 (66.7)
Agree	-	-	-
Strongly agree	3 (50.0)	3 (100.0)	-
Acceptability, mean (SD)	3.87 (1.14)	4.87 (0.12)	2.87 (0.50)
I was satisfied with the information presented about community pharmacists' role and scope			
Strongly disagree	-	-	-
Disagree	1 (16.7)	-	1 (33.3)
Neither agree nor disagree	1 (16.7)	-	1 (33.3)
Agree	2 (33.3)	1 (33.3)	1 (33.3)
Strongly agree	2 (33.3)	2 (66.7)	-
I was satisfied with the information presented about pharmacy-based naloxone service structures			
Strongly disagree	-	-	-
Disagree	2 (33.3)	-	2 (66.7)
Neither agree nor disagree	-	-	-
Agree	2 (33.3)	1 (33.3)	1 (33.3)
Strongly agree	2 (33.3)	2 (66.7)	-
I was satisfied with the information presented about pharmacy-based naloxone service processes			
Strongly disagree	-	-	-
Disagree	2 (33.3)	-	2 (66.7)
Neither agree nor disagree	-	-	-
Agree	1 (16.7)	-	1 (33.3)
Strongly agree	3 (50.0)	3 (100.0)	-

I was satisfied with the implementation resources provided in Module 2			
Strongly disagree	-	-	-
Disagree	-	-	-
Neither agree nor disagree	2 (16.7)	-	2 (66.7)
Agree	1 (50.0)	-	1 (33.3)
Strongly agree	3 (50.0)	3 (100.0)	-
I was satisfied with the information presented in Module 2 overall			
Strongly disagree	-	-	-
Disagree	1 (16.7)	-	1 (33.3)
Neither agree nor disagree	2 (33.3)	-	2 (66.7)
Agree	-	-	-
Strongly agree	3 (50.0)	3 (100.0)	-
Usability, mean (SD)	4.17 (0.96)	4.94 (0.10)	3.39 (0.67)
The information presented in Module 2 was accurate			
Strongly disagree	-	-	-
Disagree	-	-	-
Neither agree nor disagree	2 (33.3)	-	2 (66.7)
Agree	2 (33.3)	1 (33.3)	1 (33.3)
Strongly agree	2 (33.3)	2 (66.7)	-
The information in Module 2 was presented in sufficient detail			
Strongly disagree	-	-	-
Disagree	2 (33.3)	-	2 (66.7)
Neither agree nor disagree	1 (16.7)	-	1 (33.3)
Agree	-	-	-
Strongly agree	3 (50.0)	3 (100.0)	-
The text in Module 2 was easy to read			
Strongly disagree	-	-	-
Disagree	1 (16.7)	-	1 (33.3)
Neither agree nor disagree	1 (16.7)	-	1 (33.3)
Agree	1 (16.7)	-	1 (33.3)
Strongly agree	3 (50.0)	3 (100.0)	-
The text in Module 2 loaded well on my device			
Strongly disagree	-	-	-
Disagree	-	-	-
Neither agree nor disagree	-	-	-
Agree	2 (33.3)	-	2 (66.7)

Strongly agree	4 (66.7)	3 (100.0)	1 (33.3)
The graphics in Module 2 loaded well on my device			
Strongly disagree	-	-	-
Disagree	-	-	-
Neither agree nor disagree	-	-	-
Agree	2 (33.3)	-	2 (66.7)
Strongly agree	4 (66.7)	3 (100.0)	1 (33.3)
The overall appearance of Module 2 was pleasing to the eye			
Strongly disagree	-	-	-
Disagree	2 (33.3)	-	2 (66.7)
Neither agree nor disagree	-	-	-
Agree	-	-	-
Strongly agree	4 (66.7)	3 (100.0)	1 (33.3)

171

Table 4.18c Round 1 Feedback: Frequency of Panelists' Ratings Regarding Training Program Feasibility, Acceptability, and Usability in Module 3

Module 3	All (N=6) n (%)	Community Pharmacists (N=3) n (%)	Experts (N=3) n (%)
Feasibility, mean (SD)	4.50 (0.55)	5.00 (0)	4.00 (0)
The information presented in Module 3 was useful for practicing Alabama community pharmacists			
Strongly disagree	-	-	-
Disagree	-	-	-
Neither agree nor disagree	-	-	-
Agree	3 (50.0)	-	3 (100.0)
Strongly agree	3 (50.0)	3 (100.0)	-
Acceptability, mean (SD)	4.33 (0.62)	4.87 (0.23)	3.80 (0.20)
I was satisfied with the information presented about types of communication approaches			
Strongly disagree	-	-	-
Disagree	-	-	-
Neither agree nor disagree	-	-	-
Agree	4 (66.7)	1 (33.3)	3 (100.0)
Strongly agree	2 (33.3)	2 (66.7)	-
I was satisfied with the information presented about creating a culture of safety			
Strongly disagree	-	-	-
Disagree	-	-	-
Neither agree nor disagree	1 (16.7)	-	1 (33.3)
Agree	2 (33.3)	-	2 (66.7)
Strongly agree	3 (50.0)	3 (100.0)	-
I was satisfied with the information presented about using elements of motivational interviewing (MI)			
Strongly disagree	-	-	-
Disagree	1 (16.7)	-	1 (33.3)
Neither agree nor disagree	-	-	-
Agree	3 (50.0)	1 (33.3)	2 (66.7)
Strongly agree	2 (33.3)	2 (66.7)	-
I was satisfied with the language used in communication examples			
Strongly disagree	-	-	-

Disagree	-	-	-
Neither agree nor disagree	-	-	-
Agree	3 (50.0)	-	3 (100.0)
Strongly agree	3 (50.0)	3 (100.0)	-
I was satisfied with the information presented in Module 3 overall			
Strongly disagree	-	-	-
Disagree	-	-	-
Neither agree nor disagree	-	-	-
Agree	3 (50.0)	-	3 (100.0)
Strongly agree	3 (50.0)	3 (100.0)	-
Usability, mean (SD)	4.31 (0.79)	4.94 (0.10)	3.67 (0.58)
The information presented in Module 3 was accurate			
Strongly disagree	-	-	-
Disagree	-	-	-
Neither agree nor disagree	-	-	-
Agree	3 (50.0)	-	3 (100.0)
Strongly agree	3 (50.0)	3 (100.0)	-
The information in Module 3 was presented in sufficient detail			
Strongly disagree	-	-	-
Disagree	1 (16.7)	-	1 (33.3)
Neither agree nor disagree	-	-	-
Agree	3 (50.0)	1 (33.3)	2 (66.7)
Strongly agree	2 (33.3)	2 (66.7)	-
The text in Module 3 was easy to read			
Strongly disagree	-	-	-
Disagree	1 (16.7)	-	1 (33.3)
Neither agree nor disagree	-	-	-
Agree	2 (33.3)	-	2 (66.7)
Strongly agree	3 (50.0)	3 (100.0)	-
The text in Module 3 loaded well on my device			
Strongly disagree	-	-	-
Disagree	-	-	-
Neither agree nor disagree	-	-	-
Agree	3 (50.0)	-	3 (100.0)
Strongly agree	3 (50.0)	3 (100.0)	-
The graphics in Module 3 loaded well on my device			

Strongly disagree	-	-	-
Disagree	-	-	-
Neither agree nor disagree	-	-	-
Agree	3 (50.0)	-	3 (100.0)
Strongly agree	3 (50.0)	3 (100.0)	-
The overall appearance of Module 3 was pleasing to the eye			
Strongly disagree	-	-	-
Disagree	1 (16.7)	-	1 (33.3)
Neither agree nor disagree	-	-	-
Agree	2 (33.3)	-	2 (66.7)
Strongly agree	3 (50.0)	3 (100.0)	-

Based on feedback in Round 1, the training program format and content was modified by LAH, targeting items in each module to which any panelists disagreed or strongly disagreed. Free-response / text entry items allowed panelists to elaborate and comment on their ratings of each module item, and provided context for modification. Formatting was changed to incorporate more figures, larger font size, and less verbose text per slide. Content was added or modified based on panelist comments and their recommended literature and resources.

For Round 2, a total of 4 stakeholder panelists (n=4 specialized content experts) provided feedback based on their areas of expertise only (see Table 4.16). While feedback was provided on each module in its entirety, the PI (LAH) guided discussion of each module to target items to which panelists disagreed or strongly disagreed in Round 1. The training program content and format was then modified based on content expert feedback (all suggestions were minor content additions/deletions or readjustment of slide layout), and the training program was finalized. The final format and content of the training program are described in more detail in the following section (Section 4.1.6).

4.1.6 Finalized Training Program

After 2 rounds of iterative feedback and modification, the EmpoweringCommunityPharmacists training program was finalized in terms of its format and content. Details regarding the final format and content are presented below (Table 4.19).

4.1.6.1 Format

The finalized training program was formatted as a live online webinar entitled "*Naloxone – A Guide for Alabama Community Pharmacists*" and lasting 1.5 hours in length, with 30

175

minutes dedicated to each of Modules 1, 2, and 3, respectively. Zoom webinar software was used to deliver the live online session, with 1-2 audience response questions per module built in for engagement. Live webinar attendees were able to respond to questions or pose their own questions through the Zoom chat feature, and the software also allowed the session to be recorded for later viewing. For those unable to attend the live session, the webinar was recorded in order to be watched later for home-study credit. The webinar was accredited by the ACPE to provide 1.5 hours of pharmacist CE credit, both live (ACPE # Module 1: 0001-0000-18-066-L01-P, Module 2: 0001-0000-18-067-L01-P, and Module 3: 0001-0000-18-068-L01-P) and home-study (ACPE # Module 1: 0001-0000-18-069-H01-P, Module 2: 0001-0000-18-070-H01-P, and Module 3: 0001-0000-18-071-H01-P).

Furthermore, webinar slides were formatted by LAH using a template in order to ensure a consistent and appealing presentation. The EmpoweringCommunityPharmacists logo appeared on all slides for branding purposes and to direct attendees to the study website, https://www.empoweringcommunitypharmacists.org, which contained information about study milestones such as survey deadlines. At the conclusion of the study, the webinar slides were also posted to the website so all study participants could have access to the resources provided therein.

4.1.6.2 Content

The webinar content was divided into 3 modules: Module 1) Naloxone Basics and Alabama Legalities; Module 2) Practical Implementation Strategies; and Module 3) Communication Strategies. Content was delivered by 3 expert speakers (see Table 4.16) in order

to increase the validity of the program. Details of each module are summarized below (Table 4.19); see Appendix F for the full webinar slides, content, and speaker credentials.

Module 1: Naloxone Basics and Alabama Legalities

Module 1 focused on naloxone basics and Alabama legalities. Topics included general opioid overdose statistics, a review of pain management and harm reduction strategies, the CDC opioid prescribing guidelines, naloxone mechanism of action and device review, and review of Alabama's statewide standing order for naloxone. Pre-recorded videos were used to demonstrate how to administer Narcan® and Evzio® dosage forms, and training devices for these formulations were mailed to study participants ahead of time so they could follow along with the videos and practice their administration skills during the live webinar.

Module 2: Practical Implementation Strategies

Module 2 focused on practical naloxone service implementation strategies for the community pharmacy setting. Topics included how to develop a naloxone service protocol, goal setting, choosing a champion, marketing (ex. personal selling), patient identification (ex. chart review, screening forms), and documentation and follow-up with patients and providers. Resources for routinization were provided via links within the webinar slides, including protocol templates and Gantt charts. These resources were also provided to the participants via email at 1 and 2 months post-webinar for the intervention group or at study conclusion for the control group.

Module 3: Communication Strategies

Module 3 focused on communication strategies to use in the community pharmacy

setting. Topics included elements and spirit of motivational interviewing, safety-centered

language, "Go-To" phrases, and communication aids/resources for patients. Role-play scenarios

were also provided via pre-recorded videos as well as a live demonstration by the speaker.

Table 4.19 Summary of Finalized Training Program Content and Format

	Module 1 **Naloxone Basics**	**Module 2** **Implementation Strategies**	**Module 3** **Communication Strategies**
Content	**Education** • Opioid overdose statistics • Pain management & harm reduction review • Centers for Disease Control & Prevention opioid prescribing guidelines • Naloxone mechanism of action & device review • Alabama's statewide standing order **Skills Practice** • Naloxone administration workshop [a]	**Education** • Developing a naloxone protocol • Goal setting • Choosing a champion • Marketing (ex. personal selling) • Patient identification (chart review, screening) • Documentation & follow-up **Routinization Resources** • Protocol template • Gantt chart	**Education** • Motivational interviewing (ex. asking permission, rolling with resistance) • Safety-centered language • "Go-to" phrases • Communication aids (resources for patients) **Skills Practice** • Role play scenarios
Format	• Logistics: 30 minutes, Zoom webinar software, live • Appearance: branding, appeal, readability, template • Workshop: pre-recorded video and live remote follow-along [a]	• Logistics: 30 minutes, Zoom webinar software, live • Appearance: branding, appeal, readability, template • Resources: provided via study website, email, webinar links	• Logistics: 30 minutes, Zoom webinar software, live • Appearance: branding, appeal, readability, template • Role play: pre-recorded video and live demonstration
[a] Naloxone training devices mailed to participants ahead of time. Obtained from Narcan® manufacturer (ADAPT Pharma, Inc.) and Evzio® manufacturer (Kaleo, Inc.).			

4.2 <u>Specific Aim 2</u>: To evaluate a targeted naloxone training program among community pharmacists in Alabama.

The finalized EmpoweringCommunityPharmacistss training program developed in Aim 1 was implemented and delivered to Alabama community pharmacists in priority counties in Aim 2. As described previously in the Approach section, Aim 2 was conducted as a pragmatic randomized controlled trial over 3 months, with measures collected via online survey at baseline (O1), immediately post-training (O2), and 3 months (O3).

In the following sections, the results from Aim 2 are described, beginning with study enrollment and baseline demographics. Next, changes in knowledge, intentions, beliefs, and behavior over 3 months are reported. Finally, the association of knowledge, intentions, and beliefs with behaviors is assessed. The association between motivation factors and intention to provide naloxone services at baseline is also assessed.

4.2.1 Study Enrollment

The study screening and recruitment process took place over a 2-month rolling enrollment window. As described in the Approach section, pharmacists were recruited from priority counties in Alabama with the highest opioid overdose mortality rates. Due to slower than desired recruitment during the first month, initial priority counties were expanded to include 20 Alabama counties overall: Jefferson, Escambia, Baldwin, Walker, Blount, Mobile, Shelby, or Madison, St. Clair, Cullman, Cleburne, Bibb, Marshall, DeKalb, Lawrence, Franklin, Etowah, Calhoun, Cherokee, and Morgan Counties. Additional counties were purposively selected to include those with highest opioid overdose mortality rates. In total over the 2-month window, 108 Alabama pharmacists were screened for study eligibility using the online interest form

(Figure 4.3). Of these, 16 did not meet the inclusion criteria for the study (they did not work full-time in a community pharmacy setting located in a county of interest), while 92 were eligible for study participation. After contacting these 92 pharmacists by phone, email, and/or fax, 75 individuals enrolled in the study by completing the written informed consent and were randomized to either control (n=36) or intervention (n=39) after stratifying by pharmacy type.

Out of the 75 individuals who enrolled in the study, 8 were lost to follow-up (n=3 control, n=5 intervention) and 3 did not complete the baseline survey (n=1 control, n=2 intervention), leaving 64 participants (n=32 control, n=32 intervention) at baseline. Regarding data collection, there were 64 respondents to the baseline survey at O1 (n=32 control, n=32 intervention), 62 respondents to the survey at O2 (n=30 control, n=32 intervention), and 60 respondents to the survey at O3 (n=30 control, n=30 intervention). However, some individuals did not complete surveys at all 3 time points; for example, some completed the survey at O3 or O2 but did not complete the baseline survey, or vice versa. Overall, 60 participants (n=30 control, n=30 intervention) provided data at both O1 and O2, 57 participants (n=29 control, n=28 intervention) provided data at both O1 and O3, and 55 participants (n=28 control, n=27 intervention) provided data at all 3 time points.
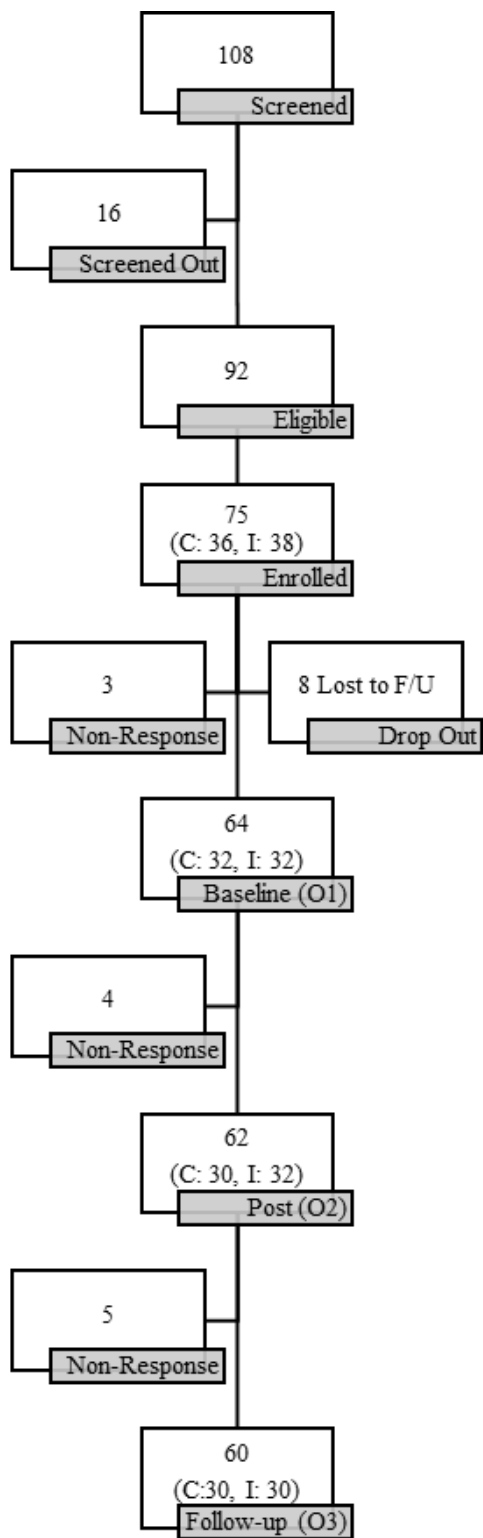
Figure 4.3 Participant Enrollment, Retention, and Participation Over 3-Month Study Period

4.2.2 Baseline Demographics

There were 64 participants (n=32 control, n=32 intervention) at baseline (O1). Their demographic information was analyzed descriptively and is presented below in terms of respondent characteristics and naloxone services at baseline.

4.2.2.1 Respondent Characteristics

Most participants were female (80.3%), white (80.6%), and worked in independently-owned pharmacies (39.1%) in urban locations (84.4%) (Table 4.20). The majority were staff pharmacists (54.1%), held a PharmD degree (73.4%), and had been practicing pharmacy for about 16 years on average, with a mean age of 42 years of age. The mean (SD) daily prescription volume was 257 (164), with a mean (SD) of 36 (51) opioid prescriptions dispensed daily. In comparing the intervention and control groups at baseline, pharmacists in the intervention group had a statistically significant higher number of years practicing pharmacy compared to the control group (p=0.021). As assessed by two-sided Mann Whitney U test for continuous variables and Fisher's Exact test for categorical variables, there were no other statistically significant differences between groups at baseline.

Table 4.20 Pharmacist Characteristics at Baseline (N=64)

Characteristics	n (%)[a]		
	All (N=64)	Control (N=32)	Intervention (N=32)
Sex			
Male	12 (19.7)	6 (19.4)	6 (19.4)
Female	49 (80.3)	25 (80.6)	24 (77.4)
Race			
White/Caucasian	50 (80.6)	25 (80.6)	25 (80.6)
Black/African American	5 (8.1)	1 (3.2)	4 (12.9)
Asian or Pacific Islander	7 (11.3)	5 (16.1)	2 (6.5)
Native American or Alaska Native	0	0	0
Ethnicity			
Hispanic origin	0	0	0
Non-Hispanic origin	61 (100.0)	31 (100.0)	30 (100.0)
Education[b]			
BSPharm	16 (25.0)	6 (19.4)	10 (32.3)
PharmD	47 (73.4)	25 (80.6)	22 (71.0)
Masters degree	0	0	0
PhD	1 (1.6)	0	1 (3.2)
Residency	5 (7.8)	2 (6.5)	3 (9.7)
Fellowship	0	0	0
Job Title			
Staff pharmacist	33 (54.1)	17 (54.8)	16 (53.3)
Pharmacist-in-charge or pharmacy manager	21 (34.4)	12 (38.7)	9 (30.0)
Pharmacy owner/partner	7 (11.5)	2 (6.5)	5 (16.7)
Community Pharmacy Practice Site			
Single-store independent	13 (20.3)	6 (18.8)	7 (21.9)
Multi-store independent	12 (18.8)	5 (15.6)	7 (21.9)
Chain	22 (34.4)	13 (40.6)	9 (28.1)
Mass merchandiser	3 (4.7)	1 (3.1)	2 (6.3)
Grocery	7 (10.9)	4 (12.5)	3 (9.4)
Embedded within a clinic	6 (9.4)	2 (6.3)	4 (12.5)
Other	1 (1.6)	1 (3.1)	0
Pharmacy Location[c]			
Urban	54 (84.4)	26 (81.3)	28 (87.5)
Rural	10 (15.6)	6 (18.8)	4 (12.5)
	Mean (SD)		
Age, years	42.1 (9.8)	40.4 (10.3)	43.7 (9.1)
Years Practicing Pharmacy*	15.9 (10.3)	13.1 (9.5)	18.6 (10.4)
Years at Current Pharmacy Site	7.3 (7.0)	7.7 (8.2)	6.9 (5.5)
FTE's Employed at Pharmacy Site[d]			
Staff pharmacists	3.2 (5.0)	2.8 (2.2)	3.5 (6.8)
Pharmacy technicians	4.6 (6.3)	4.5 (5.6)	4.6 (7.1)
Daily Number Prescriptions Dispensed			
All prescriptions	256.9 (164.0)	290.3 (174.9)	222.3 (146.9)
Opioid prescriptions	35.5 (51.0)	41.8 (61.5)	29.3 (37.7)

[a] Percentages may differ due to item non-response.

[b] Respondents were directed to select all answer choices that applied.

[c] Based on RUCA3.0 codes with 1-3=urban and 4-7=rural.

[d] FTE's = full-time equivalents.

* Statistically significant difference between groups (a priori alpha=0.05).

4.2.2.2 Naloxone Services

Over 76% of respondents offered naloxone services in their pharmacy at baseline (Table

4.21), where naloxone services were defined as any system by which the pharmacist/pharmacy

provided naloxone to potentially at-risk patients, their caregivers, or first responders. The

commercially available naloxone nasal spray (Narcan®) was the most frequently stocked dosage

form (71%), with the prefilled syringe +/- mucosal atomizer being the least frequently stocked

(11.3%). However, despite the majority of pharmacies stocking at least some form of naloxone,

only a mean (SD) of 3.1 (5.9) naloxone prescriptions were dispensed in the past 3 months at

respondents' pharmacies. As assessed by two-sided Mann Whitney U test for continuous

variables and Fisher's Exact test for categorical variables, there were no statistically significant

differences between groups at baseline.

Table 4.21 Respondents' Current Naloxone Services at Baseline (N=64)

Question	n (%)[a]		
	All (N=64)	**Control (N=32)**	**Intervention (N=32)**
Do you currently offer naloxone services at your pharmacy?			
Yes	49 (76.6)	26 (81.3)	23 (71.9)
No	15 (23.4)	6 (18.8)	9 (28.1)
During the past 3 months, which naloxone dosage forms were stocked in your pharmacy?[b]			
Nasal spray (Narcan®)	44 (71.0)	22 (71.0)	22 (71.0)
Auto-injector (Evzio®)	10 (16.1)	4 (12.9)	6 (19.4)
Vial for intramuscular (IM) injection + syringe	10 (16.1)	2 (6.5)	8 (25.8)
Pre-filled syringe +/- mucosal atomizer	7 (11.3)	2 (6.5)	5 (16.1)
	Mean (SD)		
During the past 3 months, how many naloxone prescriptions were dispensed in your pharmacy?			
Total	3.1 (5.9)	2.6 (4.4)	3.6 (7.3)
Nasal spray (Narcan®)	2.2 (4.2)	2.2 (4.3)	2.2 (4.2)
Auto-injector (Evzio®)	0.4 (1.6)	0.2 (0.6)	0.7 (2.2)
Vial for intramuscular (IM) injection + syringe	0.2 (0.9)	0.1 (0.4)	0.3 (1.2)
Pre-filled syringe +/- mucosal atomizer	0.3 (5.9)	0.2 (0.9)	0.4 (1.7)

[a] Percentages may differ due to item non-response.
[b] Respondents were directed to select all answer choices that applied.

4.2.3 Changes in Knowledge, Intentions, Beliefs, and Behaviors Over 3 Months

Our primary operating hypothesis was that receipt of a targeted naloxone training program will improve Alabama community pharmacists' perceived barriers, knowledge, attitudes, confidence, intentions, service structure and process implementation, and number of naloxone prescriptions dispensed. The following sections present respondents' knowledge about naloxone, intention to provide naloxone services, beliefs about naloxone services (attitudes, confidence, perceived barriers), and behaviors (naloxone service structure activities completed, naloxone service processes engaged in, and number of naloxone prescriptions dispensed) across the 3-month study period (H1-8a; Figure 4.4). Each construct is analyzed using descriptive statistics at O1, O2, and/or O3 depending on the time points at which they were measured, followed by analysis of changes in mean scale scores across the 3 time points using inferential statistics.
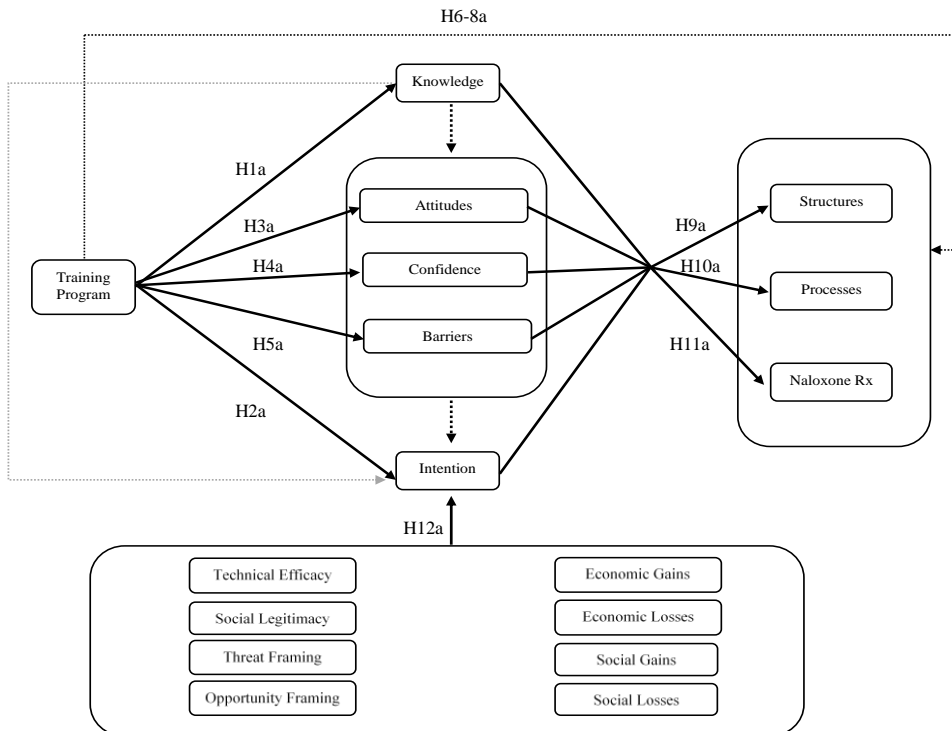
Figure 4.4 Study Conceptual Model and Hypotheses

185

Change in Knowledge

  Hypothesis 1a stated that change in naloxone knowledge from baseline to post-training and baseline to 3-months will be greater among intervention compared to control group pharmacists. To assess this, respondent knowledge about naloxone was measured at O1, O2, and O3. Internal consistency of the knowledge index was low (KR-20=0.259) (see Appendix G for a comprehensive summary of internal consistency for survey instrument constructs). Respondent knowledge is described at each time point in terms of frequency of selecting the correct response (Table 4.22). These frequencies are based on the total number of individuals who responded to the survey at each time point (O1: N=64, O2: N=62, O3: N=60).

Table 4.22 Respondent Knowledge at O1, O2, and O3

Question	Selected Correct Response(s), n (%)					
	O1 (N=64)		O2 (N=62)		O3 (N=60)	
	C (N=32)	I (N=32)	C (N=30)	I (N=32)	C (N=30)	I (N=30)
How long does naloxone take to have an effect? Correct response(s): 2-5 minutes	29 (90.6)	28 (87.5)	28 (93.3)	32 (100.0)	29 (96.7)	29 (96.7)
Where is the most recommended place for non-experts to administer naloxone? Correct response(s): Outside of thigh/upper arm (IM injection) or intranasal	15 (46.9)	25 (78.1)	21 (70.0)	28 (87.5)	26 (86.7)	29 (96.7)
For how long do the effects of naloxone last? Correct response(s): About an hour (30-90 minutes)	12 (37.5)	14 (43.8)	16 (53.3)	23 (71.9)	13 (43.3)	17 (56.7)
If the first dose of naloxone has no effect, a second dose can be given. Correct response(s): True	31 (96.9)	31 (96.9)	29 (96.7)	32 (100.0)	29 (96.7)	28 (93.3)
The effect of naloxone is shorter than the effect of heroin or methadone. Correct response(s): True	28 (87.5)	27 (84.4)	25 (83.3)	32 (100.0)	27 (90.0)	28 (93.3)
Under Alabama law, pharmacists are protected from civil and criminal liability for providing naloxone. Correct response(s): True	31 (96.9)	32 (100.0)	30 (100.0)	32 (100.0)	30 (100.0)	30 (100.0)
Commercially available forms of naloxone for outpatient pharmacy dispensing include which of the following?[a] Correct response(s): All following dosage forms	10 (31.3)	18 (56.3)	14 (46.7)	20 (62.5)	16 (53.3)	19 (63.3)
Auto-injector	*24 (75.0)*	*27 (84.4)*	*27 (90.0)*	*32 (100.0)*	*26 (86.7)*	*30 (100.0)*
Nasal spray	*30 (93.8)*	*31 (96.9)*	*30 (100.0)*	*32 (100.0)*	*30 (100.0)*	*30 (100.0)*
Injection vial + IM syringe	*16 (50.0)*	*28 (87.5)*	*19 (63.3)*	*23 (71.9)*	*19 (63.3)*	*25 (83.3)*
Prefilled syringe +/- mucosal atomizer	*19 (59.4)*	*22 (68.8)*	*18 (60.0)*	*26 (81.3)*	*22 (73.3)*	*20 (66.7)*

C=Control group, I=Intervention group

[a] Respondents were instructed to select all answer choices that applied.

Among the 55 individuals who responded to all 3 surveys, the mean knowledge score (percent correct) was above 70% for both groups at each time point (Tables 4.23a-b). Specifically, the mean (SD) knowledge score among the intervention group was 76.72% (14.90) at O1, 88.89% (11.44) at O2, and 87.30% (12.10) at O3. Among the control group, mean (SD) knowledge scores were 70.41 (13.98) at O1, 77.04 (14.20) at O2, and 81.12 (14.05) at O3.

Changes in mean knowledge scores across O1, O2, and O3 were also assessed for the 55 individuals who responded to all 3 surveys (Tables 4.23a-b, Figure 4.5). Values are mean (SD) unless stated otherwise. There was a statistically significant increase in knowledge score within the intervention group from O1 to O2 (76.72% to 88.89%, p=0.001), and this change was maintained at 3 months (O2-O3: -1.59, p=0.201). However, the change within the intervention group was not statistically significant compared to control (p=0.205). Overall, the EmpoweringCommunityPharmacists intervention did not significantly affect pharmacist knowledge about pharmacy-based naloxone services compared to control (p=0.294).

In summary, hypothesis 1a stated that change in naloxone knowledge from baseline to post-training and baseline to 3-months will be greater among intervention compared to control group pharmacists. We failed to reject the null hypothesis, and concluded that the training program had no effect on pharmacist knowledge.

Table 4.23a. Overall Effect of the Intervention on Knowledge Score

Factor	F	p-value [a]
Time	16.023	<0.0005*
Time * Group	1.237	0.294
Group	8.609	0.005*

Table 4.23b. Change in Mean Knowledge Score in Control and Intervention Groups Over 3 Months (N=55)

	Mean Knowledge Score (% Correct) at O1, O2, O3	
	Control	Intervention
Time	Mean (SD)	Mean (SD)
O1	70.41 (13.98)	76.72 (14.90)
O2	77.04 (14.20)	88.89 (11.44)
O3	81.12 (14.05)	87.30 (12.10)

	Change in Knowledge Score (% Correct) Within Groups				Between Groups
	Control (N=28)		Intervention (N=27)		
Time	Mean Difference (SE)	p-value [a]	Mean Difference (SE)	p-value [a]	p-value [a]
O1-O2	6.63 (3.02)	0.098	12.17 (3.08)	0.001*	0.205
O2-O3	4.08 (3.07)	0.567	-1.59 (3.12)	1.000	0.201
O1-O3	10.71 (2.53)	<0.0005*	10.58 (2.57)	<0.0005*	0.971
Overall		<0.0005*		<0.0005*	0.294

Significance at the 0.05 level indicated by *.

[a] Based on results of mixed ANOVA with Bonferroni post-hoc tests.
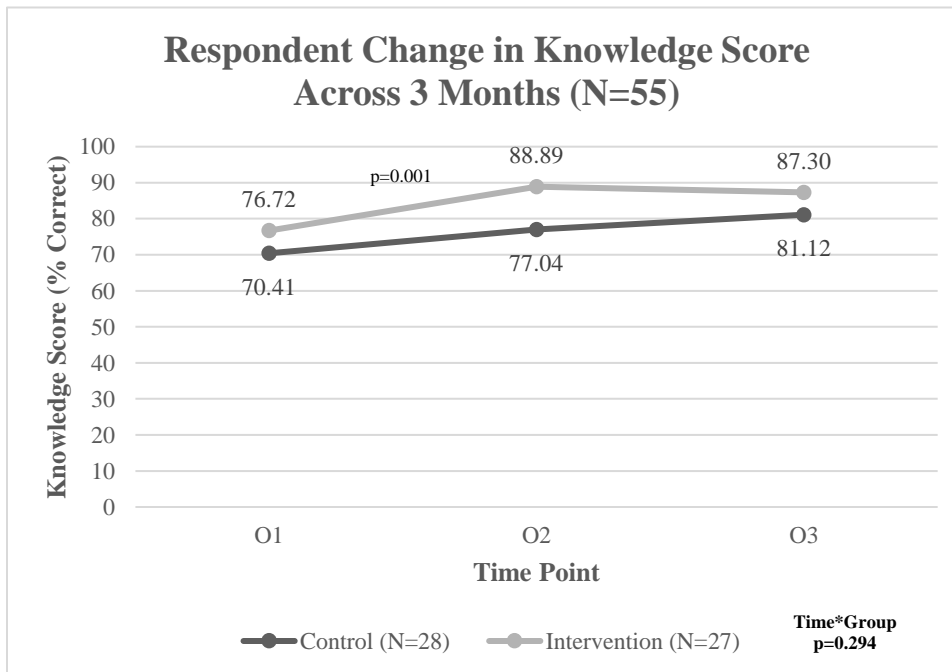
Figure 4.5 Change in Mean Knowledge Score Over 3-Month Study Period. Only statistically significant p-values within groups are shown.

Change in Intention

Hypothesis 2a stated that change in intention to dispense naloxone or perform naloxone services from baseline to post-training and baseline to 3-months will be greater among intervention compared to control group pharmacists. To assess this, respondent intention to complete/engage in naloxone service activities was measured at O1, O2, and O3. Exploratory factor analysis (EFA) showed that all scale items loaded on one factor (Intention) with eigenvalue ≥ 1. The overall intention scale had high internal consistency (Cronbach's alpha=0.853). Respondent intentions at each time point are described below in terms of frequency of agreement or disagreement to scale items (Table 4.24).

Table 4.24 Respondents' Intentions to Complete/Engage in Naloxone Service Activities at O1, O2, O3

Question [a] "In the next 3 months, I intend to…"	n (%) [b]					
	O1 (N=64)		O2 (N=62)		O3 (N=60)	
	C (N=32)	I (N=32)	C (N=30)	I (N=32)	C (N=30)	I (N=30)
Proactively identify patients who would benefit from naloxone						
Strongly disagree	0	3 (9.4)	1 (3.4)	0	1 (3.3)	2 (6.7)
Disagree	1 (3.1)	2 (6.3)	0	1 (3.1)	1 (3.3)	0
Somewhat disagree	2 (6.3)	0	2 (6.9)	0	1 (3.3)	0
Neither agree nor disagree	3 (9.4)	3 (9.4)	1 (3.4)	3 (9.4)	4 (13.3)	4 (13.3)
Somewhat agree	5 (15.6)	9 (28.1)	6 (20.7)	6 (18.8)	8 (26.7)	3 (10.0)
Agree	**11 (34.4)**	**14 (43.8)**	**15 (51.7)**	**16 (50.0)**	6 (20.0)	**16 (53.3)**
Strongly agree	10 (31.3)	1 (3.1)	4 (13.8)	6 (18.8)	**9 (30.0)**	5 (16.7)
Initiate a conversation with a patient regarding the need for take-home naloxone						
Strongly disagree	0	2 (6.3)	1 (3.4)	0	1 (3.3)	1 (3.3)
Disagree	1 (3.1)	1 (3.1)	1 (3.4)	2 (6.3)	0	0
Somewhat disagree	1 (3.1)	1 (3.1)	0	0	1 (3.3)	0
Neither agree nor disagree	3 (9.4)	4 (12.5)	3 (10.3)	3 (9.4)	2 (6.7)	4 (13.3)
Somewhat agree	5 (15.6)	10 (31.3)	7 (24.10	4 (12.4)	**9 (30.0)**	2 (6.7)
Agree	**15 (46.9)**	**12 (37.5)**	**13 (44.8)**	**17 (53.1)**	8 (26.7)	**15 (50.0)**
Strongly agree	7 (21.9)	2 (6.3)	4 (13.8)	6 (18.8)	**9 (30.0)**	8 (26.7)
Stock naloxone products in my pharmacy						
Strongly disagree	1 (3.1)	2 (6.3)	1 (3.4)	0	1 (3.3)	1 (3.3)
Disagree	1 (3.1)	1 (3.1)	1 (3.4)	2 (6.3)	0	0
Somewhat disagree	0	1 (3.1)	0	1 (3.1)	1 (3.3)	0
Neither agree nor disagree	2 (6.3)	3 (9.4)	5 (17.2)	2 (6.3)	2 (6.7)	2 (6.7)
Somewhat agree	1 (3.1)	3 (9.4)	2 (6.9)	3 (9.4)	2 (6.7)	2 (6.7)
Agree	9 (28.1)	6 (18.8)	8 (27.6)	4 (12.5)	8 (26.7)	6 (20.0)
Strongly agree	**18 (56.3)**	**16 (50.0)**	**12 (41.4)**	**20 (62.5)**	**16 (53.3)**	**19 (63.3)**
Dispense naloxone if prescribed by a physician						
Strongly disagree	0	2 (6.3)	1 (3.4)	0	1 (3.3)	1 (3.3)
Disagree	0	1 (3.1)	0	1 (3.1)	0	0
Somewhat disagree	0	0	0	0	0	0
Neither agree nor disagree	0	1 (3.1)	0	1 (3.1)	0	3 (10.0)

Somewhat agree	1 (3.1)	1 (3.1)	1 (3.4)	0	0	0
Agree	6 (18.8)	5 (15.6)	6 (20.7)	8 (25.0)	5 (16.7)	7 (23.3)
Strongly agree	**25 (78.1)**	**22 (68.8)**	**21 (72.4)**	**22 (68.8)**	**24 (80.0)**	**19 (63.3)**
Dispense naloxone using Alabama's statewide standing order, if indicated						
Strongly disagree	0	2 (6.3)	1 (3.4)	0	1 (3.3)	1 (3.3)
Disagree	2 (6.3)	1 (3.1)	1 (3.4)	1 (3.1)	1 (3.3)	0
Somewhat disagree	2 (6.3)	1 (3.1)	2 (6.9)	0	2 (6.7)	0
Neither agree nor disagree	4 (12.5)	3 (9.4)	3 (10.3)	3 (9.4)	4 (13.3)	3 (10.0)
Somewhat agree	3 (9.4)	5 (15.6)	2 (6.9)	4 (12.5)	4 (13.3)	0
Agree	9 (28.1)	5 (15.6)	**13 (44.8)**	7 (21.9)	7 (23.3)	10 (33.3)
Strongly agree	**12 (37.5)**	**15 (46.9)**	7 (24.1)	**17 (53.1)**	**11 (36.7)**	**16 (53.3)**

C=Control group, I=Intervention group

[a] On a Likert-type scale of 1 to 7, where 1=strongly disagree and 7=strongly agree.

[b] Percentages may differ due to item non-response.

Among the 55 individuals who responded to all 3 surveys, the mean intention scale score was above 5.00 for both groups at each time point (Tables 4.25a-b). Specifically, the mean (SD) intention scale score among the intervention group was 5.35 (1.51) at O1, 6.10 (0.96) at O2, and 6.01 (1.22) O3. Among the control group, mean (SD) intention scores were 5.99 (0.88) at O1, 5.68 (1.18) at O2, and 5.76 (1.17) at O3.

Changes in mean intention scale score across O1, O2, and O3 were also assessed for the 55 individuals who responded to all 3 surveys (Tables 4.25a-b, Figure 4.6). Values are mean (SD) unless stated otherwise. There was a statistically significant increase in intention score within the intervention group from O1 to O2 (5.35 to 6.10, p=0.023), and this change was maintained at 3 months (O2-O3: -0.08, p=1.000). The change within the intervention group was statistically significant compared to control (p=0.008). Overall, the training program significantly affected pharmacist intention to provide naloxone services compared to control (p=0.014).

In summary, hypothesis 2a stated that change in intention to dispense naloxone or perform naloxone services from baseline to post-training and baseline to 3-months will be greater among intervention compared to control group pharmacists. We rejected the null hypothesis, and concluded that the training program had an effect on pharmacist intention.

Table 4.25a. Overall Effect of the Intervention on Intention

Factor	F	p-value [a]
Time	0.920	0.402
Time * Group	4.480	0.014*
Group	0.002	0.966

Table 4.25b. Change in Mean Intention Scale Score in Control and Intervention Groups Over 3 Months (N=55)

	Mean Intention Scale Scores at O1, O2, O3					
	Control			Intervention		
Time	Mean (SD)			Mean (SD)		
O1	5.99 (0.88)			5.35 (1.51)		
O2	5.68 (1.18)			6.10 (0.96)		
O3	5.76 (1.17)			6.01 (1.22)		
	Change in Intention Within Groups					Between
	Control (N=28)		Intervention (N=27)			Groups
Time	Mean Difference (SE)	p-value [a]	Mean Difference (SE)	p-value [a]		p-value [a]
O1-O2	0.30 (0.27)	0.793	0.75 (0.27)	0.023*		0.008*
O2-O3	-0.08 (0.26)	1.000	-0.08 (0.26)	1.000		0.658
O1-O3	0.22 (0.27)	1.000	0.67 (0.27)	0.056		0.026*
Overall		0.526		0.018*		0.014*

Significance at the 0.05 level indicated by *.
[a] Based on results of mixed ANOVA with Bonferroni post-hoc tests.
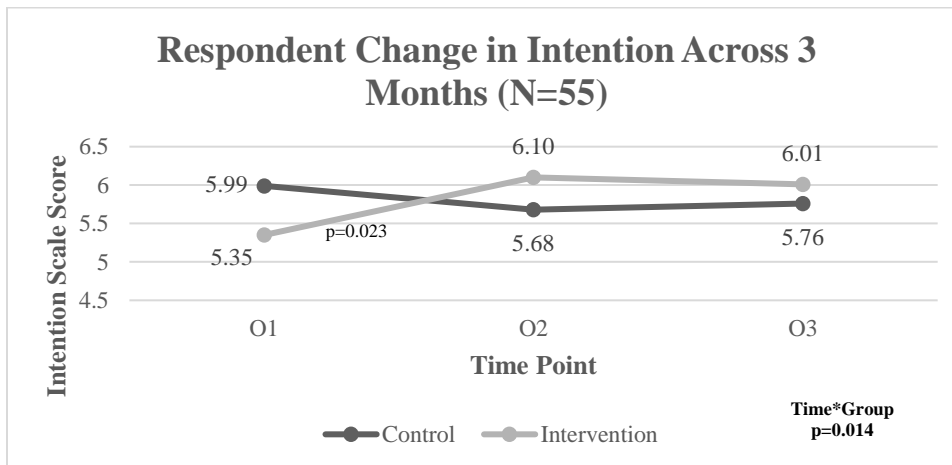
Figure 4.6 Change in Mean Intention Scale Score Over 3-Month Study Period. Only statistically significant p-values within groups are shown.

Change in Beliefs

   Hypotheses 3a, 4a, and 5a stated that change in attitudes, confidence, and perceived barriers regarding naloxone services from baseline to post-training and baseline to 3-months will be greater among intervention compared to control group pharmacists, respectively. To assess these hypotheses, beliefs were measured at O1, O2, and O3 and included attitudes about pharmacy-based naloxone services, confidence regarding providing pharmacy-based naloxone services, and perceived barriers to providing pharmacy-based naloxone services. Each construct is presented separately below.

Attitudes

   The overall attitude scale had high internal consistency (Cronbach's alpha=0.847). Exploratory factor analysis (EFA) showed that pharmacy-based naloxone service attitudes was composed of 2 factors with eigenvalues >1: Attitudes Regarding Illicit Opioid Misuse (Cronbach's alpha=0.725); and Attitudes Regarding Prescription Opioid Misuse (Cronbach's alpha=0.820) (see Appendix H). Respondent attitudes at each time point are described below in terms of frequency of agreement or disagreement to scale items (Table 4.26).

Table 4.26 Respondent Attitudes at O1, O2, O3

Question [a]	n (%) [b]					
	O1 (N=64)		O2 (N=62)		O3 (N=60)	
	C (N=32)	I (N=32)	C (N=30)	I (N=32)	C (N=30)	I (N=30)
Attitudes Regarding Illicit Opioid Misuse						
People who inject illicit opioid drugs visiting my pharmacy would have a damaging effect on business [c]						
Strongly disagree	2 (6.3)	**8 (25.0)**	4 (13.8)	6 (18.8)	3 (10.0)	4 (13.3)
Disagree	**12 (37.5)**	6 (18.8)	**8 (27.6)**	7 (21.9)	9 (30.0)	**11 (36.7)**
Somewhat disagree	3 (9.4)	6 (18.8)	3 (10.3)	7 (21.9)	3 (10.0)	0
Neither agree nor disagree	7 (21.9)	3 (9.4)	5 (17.2)	**8 (25.0)**	**8 (26.7)**	10 (33.3)
Somewhat agree	5 (15.6)	6 (18.8)	5 (17.2)	3 (9.4)	3 (10.0)	2 (6.7)
Agree	2 (6.3)	2 (6.3)	3 (10.3)	1 (3.1)	4 (13.3)	1 (3.3)
Strongly agree	1 (3.1)	1 (3.1)	1 (3.4)	0	0	2 (6.7)
It is appropriate for pharmacists to provide naloxone to people who inject illicit opioids						
Strongly disagree	0	0	0	0	0	2 (6.7)
Disagree	0	0	2 (6.9)	2 (6.3)	0	0
Somewhat disagree	2 (6.3)	5 (15.6)	2 (6.9)	1 (3.1)	2 (6.7)	0
Neither agree nor disagree	5 (15.6)	2 (6.3)	4 (13.8)	3 (9.4)	0	3 (10.0)
Somewhat agree	4 (12.5)	5 (15.6)	3 (10.3)	5 (15.6)	5 (16.7)	5 (16.7)
Agree	**14 (43.8)**	**10 (31.3)**	**12 (41.4)**	10 (31.3)	**16 (53.3)**	**11 (36.7)**
Strongly agree	7 (21.9)	**10 (31.3)**	6 (20.7)	**11 (34.4)**	7 (23.3)	9 (30.0)
It is appropriate for pharmacists to contact physicians to obtain a naloxone prescription for eligible patients						
Strongly disagree	0	1 (3.1)	0	0	0	0
Disagree	1 (3.1)	1 (3.1)	2 (6.9)	3 (9.4)	2 (6.7)	1 (3.3)
Somewhat disagree	1 (3.1)	1 (3.1)	1 (3.4)	0	0	0
Neither agree nor disagree	1 (3.1)	2 (6.3)	3 (10.3)	5 (15.6)	0	4 (13.3)
Somewhat agree	0	5 (15.6)	3 (10.3)	2 (6.3)	4 (13.3)	3 (10.0)
Agree	**23 (71.9)**	9 (28.1)	**11 (37.9)**	10 (31.3)	**18 (60.0)**	10 (33.3)
Strongly agree	6 (18.8)	**13 (40.6)**	9 (31.0)	**12 (37.5)**	6 (20.0)	**12 (40.0)**
I have no sympathy for people who misuse opioids [c]						
Strongly disagree	**13 (40.6)**	**14 (43.8)**	**12 (41.4)**	**13 (40.6)**	**11 (36.7)**	10 (33.3)
Disagree	12 (37.5)	7 (21.9)	8 (27.6)	12 (37.5)	9 (30.0)	**10 (33.3)**

Somewhat disagree	1 (3.1)	4 (12.5)	3 (10.3)	2 (6.3)	4 (13.3)	1 (3.3)
Neither agree nor disagree	1 (3.1)	4 (12.5)	2 (6.9)	4 (12.5)	3 (10.0)	6 (20.0)
Somewhat agree	3 (9.4)	3 (9.4)	1 (3.4)	1 (3.1)	2 (6.7)	1 (3.3)
Agree	2 (6.3)	0	3 (10.3)	0	0	1 (3.3)
Strongly agree	0	0	0	0	1 (3.3)	1 (3.3)
I feel comfortable supplying naloxone to people who inject illicit opioids						
Strongly disagree	0	1 (3.1)	2 (6.9)	2 (6.3)	1 (3.3)	1 (3.3)
Disagree	2 (6.3)	4 (12.5)	1 (3.4)	1 (3.1)	2 (6.7)	1 (3.3)
Somewhat disagree	5 (15.6)	2 (6.3)	4 (13.8)	1 (3.1)	2 (6.7)	0
Neither agree nor disagree	5 (15.6)	4 (12.5)	2 (6.9)	5 (15.6)	4 (13.3)	5 (16.7)
Somewhat agree	6 (18.8)	**9 (28.1)**	7 (24.1)	8 (25.0)	6 (20.0)	7 (23.3)
Agree	**8 (25.0)**	7 (21.9)	**8 (27.6)**	**9 (28.1)**	**8 (26.7)**	**8 (26.7)**
Strongly agree	6 (18.8)	5 (15.6)	5 (17.2)	6 (18.8)	7 (23.3)	**8 (26.7)**
Attitudes Regarding Prescription Opioid Misuse						
Supplying naloxone in pharmacies encourages inappropriate use of opioids [c]						
Strongly disagree	**12 (37.5)**	**12 (37.5)**	**10 (34.5)**	**14 (43.8)**	**13 (43.3)**	**13 (43.3)**
Disagree	13 (40.6)	10 (31.3)	9 (31.0)	11 (34.40	12 (40.0)	12 (40.0)
Somewhat disagree	0	4 (12.5)	2 (6.9)	2 (6.3)	2 (6.7)	1 (3.3)
Neither agree nor disagree	3 (.9.4)	2 (6.3)	4 (13.8)	2 (6.3)	1 (3.3)	2 (6.7)
Somewhat agree	3 (9.3)	2 (6.3)	2 (6.9)	3 (9.4)	1 (3.3)	2 (6.7)
Agree	0	0	1 (3.4)	0	1 (3.3)	0
Strongly agree	1 (3.1)	2 (6.3)	1 (3.4)	0	0	0
It is unethical to supply naloxone to people who use opioids [c]						
Strongly disagree	**17 (53.1)**	**20 (62.5)**	**15 (51.7)**	**23 (71.9)**	**15 (50.0)**	**17 (56.7)**
Disagree	12 (37.5)	9 (28.1)	13 (44.8)	7 (21.9)	13 (43.3)	12 (40.0)
Somewhat disagree	1 (3.1)	2 (6.3)	1 (3.4)	1 (31.)	0	0
Neither agree nor disagree	1 (3.1)	1 (3.1)	0	1 (3.1)	1 (3.3)	1 (3.3)
Somewhat agree	1 (3.1)	0	0	0	0	0
Agree	0	0	0	0	1 (3.3)	0
Strongly agree	0	0	0	0	0	0
It is part of a pharmacists' professional duty to provide naloxone to people who use opioids						
Strongly disagree	0	1 (3.1)	1 (3.4)	1 (3.1)	0	0
Disagree	1 (3.1)	3 (9.4)	2 (6.9)	0	0	0

197

Somewhat disagree	1 (3.1)	4 (12.5)	1 (3.4)	0	0	0
Neither agree nor disagree	3 (9.4)	4 (12.5)	2 (6.9)	5 (15.6)	6 (20.0)	5 (16.7)
Somewhat agree	7 (21.9)	2 (6.3)	4 (13.8)	5 (15.6)	5 (16.7)	5 (16.7)
Agree	**13 (40.6)**	8 (25.0)	**13 (44.8)**	**13 (40.6)**	**10 (33.3)**	**10 (33.3)**
Strongly agree	7 (21.9)	**10 (31.3)**	6 (20.7)	8 (25.0)	9 (30.0)	**10 (33.3)**
People who take high-dose opioid prescriptions visiting my pharmacy would have a damaging effect on business [c]						
Strongly disagree	3 (9.4)	**11 (34.4)**	7 (24.1)	8 (25.0)	5 (16.7)	7 (23.3)
Disagree	**20 (62.5)**	**11 (34.4)**	**12 (41.4)**	**12 (37.5)**	**15 (50.0)**	**11 (36.7)**
Somewhat disagree	1 (3.1)	6 (18.8)	4 (13.8)	5 (15.6)	2 (6.7)	2 (6.7)
Neither agree nor disagree	6 (18.8)	3 (9.4)	4 (13.8)	7 (21.9)	7 (23.3)	7 (23.3)
Somewhat agree	1 (3.1)	0	2 (6.9)	0	0	3 (10.0)
Agree	0	1 (3.1)	0	0	1 (3.3)	0
Strongly agree	1 (3.1)	0	0	0	0	0
It is appropriate for pharmacists to provide naloxone to people who use prescription opioids						
Strongly disagree	0	0	0	1 (3.1)	0	0
Disagree	0	0	0	0	0	0
Somewhat disagree	0	1 (3.1)	0	0	0	0
Neither agree nor disagree	1 (3.1)	1 (3.1)	1 (3.4)	1 (3.1)	0	1 (3.3)
Somewhat agree	2 (6.3)	5 (15.6)	1 (3.4)	4 (12.5)	4 (13.3)	2 (6.7)
Agree	**21 (65.6)**	7 (21.9)	**14 (48.3)**	10 (31.3)	**15 (50.0)**	12 (40.0)
Strongly agree	8 (25.0)	**18 (56.3)**	13 (44.8)	**16 (50.0)**	11 (36.7)	**15 (50.0)**
Supplying naloxone at the pharmacy will help reduce opioid overdose deaths						
Strongly disagree	0	0	0	0	0	1 (3.3)
Disagree	1 (3.1)	2 (6.3)	0	2 (6.3)	0	1 (3.3)
Somewhat disagree	0	0	0	0	0	1 (3.3)
Neither agree nor disagree	3 (9.4)	1 (3.1)	3 (10.3)	0	4 (13.3)	1 (3.3)
Somewhat agree	3 (9.4)	6 (18.8)	3 (10.3)	7 (21.9)	2 (6.7)	1 (3.3)
Agree	**15 (46.9)**	**12 (37.5)**	**13 (44.8)**	**12 (37.5)**	**16 (53.3)**	**14 (46.7)**
Strongly agree	10 (31.3)	11 (34.4)	10 (34.5)	11 (34.4)	8 (26.7)	11 (36.7)
Offering naloxone in pharmacies is a good use of time and money						
Strongly disagree	0	0	0	0	0	0
Disagree	0	2 (6.3)	1 (3.4)	0	1 (3.3)	0

Somewhat disagree	2 (6.3)	1 (3.1)	3 (10.3)	1 (3.1)	1 (3.3)	1 (3.3)
Neither agree nor disagree	7 (21.9)	4 (12.5)	3 (10.3)	3 (9.4)	8 (26.7)	1 (3.3)
Somewhat agree	5 (15.6)	6 (18.8)	3 (10.3)	5 (15.6)	3 (10.0)	6 (20.0)
Agree	**14 (43.8)**	**13 (40.6)**	**12 (41.4)**	**15 (46.9)**	**12 (40.0)**	**15 (50.0)**
Strongly agree	4 (12.5)	6 (18.8)	7 (24.1)	8 (25.0)	5 (16.7)	7 (23.3)
Pharmacists have a role to play in opioid overdose prevention						
Strongly disagree	0	1 (3.1)	0	0	0	0
Disagree	0	0	0	0	0	0
Somewhat disagree	0	0	0	0	0	0
Neither agree nor disagree	0	0	1 (3.4)	1 (3.1)	0	1 (3.3)
Somewhat agree	1 (3.1)	8 (25.0)	3 (10.3)	0	6 (20.0)	3 (10.0)
Agree	14 (43.8)	8 (25.0)	**14 (48.3)**	15 (46.9)	**12 (40.0)**	**13 (43.3)**
Strongly agree	**17 (53.1)**	**15 (46.9)**	11 (37.9)	**16 (50.0)**	**12 (40.0)**	**13 (43.3)**
Other pharmacists will support my decision to supply naloxone in my pharmacy						
Strongly disagree	1 (3.1)	1 (3.1)	0	0	0	0
Disagree	0	0	0	0	0	0
Somewhat disagree	0	0	1 (3.4)	1 (3.1)	1 (3.3)	1 (3.3)
Neither agree nor disagree	3 (9.4)	3 (9.4)	3 (10.3)	2 (6.3)	2 (6.7)	3 (10.0)
Somewhat agree	2 (6.3)	7 (21.9)	5 (17.2)	3 (9.4)	2 (6.7)	1 (3.3)
Agree	**15 (46.9)**	**12 (37.5)**	**13 (44.8)**	**16 (50.0)**	**16 (53.3)**	**16 (53.3)**
Strongly agree	11 (34.4)	9 (28.1)	7 (24.1)	10 (31.3)	9 (30.0)	9 (30.0)
I feel comfortable supplying naloxone to people who take high-dose opioid prescriptions						
Strongly disagree	1 (3.1)	0	0	0	0	0
Disagree	0	2 (6.3)	1 (3.4)	0	0	0
Somewhat disagree	0	0	0	1 (3.1)	1 (3.3)	0
Neither agree nor disagree	1 (3.1)	2 (6.3)	1 (3.4)	2 (6.3)	1 (3.3)	1 (3.3)
Somewhat agree	1 (3.1)	5 (15.6)	3 (10.3)	2 (6.3)	5 (16.7)	4 (13.3)
Agree	**15 (46.9)**	11 (34.4)	**16 (55.2)**	**16 (50.0)**	11 (36.7)	12 (40.0)
Strongly agree	14 (43.8)	**12 (37.5)**	8 (27.6)	11 (34.4)	**12 (40.0)**	**13 (43.3)**

C=Control group, I=Intervention group

[a] On a Likert-type scale of 1 to 7, where 1=strongly disagree and 7=strongly agree.

[b] Percentages may differ due to item non-response.

[c] Reverse coded items.

Items were reverse coded when necessary so that higher mean scale scores aligned with more positive attitudes towards pharmacy-based naloxone services. Reverse coded items are indicated in the table above (Table 4.26). Among the 55 individuals who responded to all 3 surveys, the mean overall attitude scale score was above 5.00 for both groups at each time point (Tables 4.27a-b). Specifically, the mean (SD) overall attitude scale score among the intervention group was 5.66 (0.90) at O1, 5.94 (0.62) at O2, and 5.92 (0.71) O3. Among the control group, mean (SD) overall attitude scores were 5.72 (0.68) at O1, 5.66 (0.81) at O2, and 5.75 (0.72) at O3. Similar patterns were seen for attitudes regarding illicit opioid misuse and attitudes regarding prescription opioid misuse, with mean scale scores for attitudes towards illicit misuse being generally lower and attitudes towards prescription misuse being generally higher.

Changes in mean overall attitude scale scores across O1, O2, and O3 were also assessed for the 55 individuals who responded to all 3 surveys (Tables 4.27a-b, Figure 4.7). Values are mean (SD) unless stated otherwise. There was a statistically significant increase in overall attitude scale score within the intervention group from O1 to O3 (5.66 to 5.92, p=0.046) but not O1 to O2 (p=0.050). However, this change was not statistically significant compared to control (p=0.128).

Furthermore, for attitudes regarding illicit versus prescription opioid misuse, attitudes tended to be lower (more negative) for the illicit category compared to the prescription category in each group. For attitudes regarding illicit opioid misuse, there was no statistically significant change in attitudes in either the control or intervention over 3 months. There was a statistically significant increase in the attitudes regarding prescription opioid misuse scale score within the intervention group from O1 to O3 (5.82 to 6.12, p=0.022) but not O1 to O2 (p=0.057). However, this change was not statistically significant compared to control (p=0.084). Overall,

compared to control, the training program did not affect pharmacists' positive attitudes towards pharmacy-based naloxone services (p=0.061), pharmacists' attitudes towards illicit opioid misuse (p=0.157), or attitudes towards prescription opioid misuse (p=0.094).

In summary, hypothesis 3a stated that change in attitudes regarding naloxone services from baseline to post-training and baseline to 3-months will be greater among intervention compared to control group pharmacists. We failed to reject the null hypothesis, and concluded that the training program had no effect on pharmacist attitudes.

Table 4.27a. Overall Effect of the Intervention on Attitude

Factor	F	p-value [a]
Overall Attitude		
Time	2.309	0.108
Time * Group	2.941	0.061
Group	0.487	0.488
Attitudes Regarding Illicit Opioid Misuse		
Time	0.419	0.659
Time * Group	1.885	0.157
Group	0.445	0.508
Attitudes Regarding Prescription Opioid Misuse		
Time	2.928	0.063
Time * Group	2.488	0.094
Group	0.387	0.537

Table 4.27b. Change in Mean Attitude Scale Score in Control and Intervention Groups Over 3 Months (N=55)

Overall Attitudes					
Mean Attitude Scale Scores at O1, O2, O3					
	Control		**Intervention**		
Time	**Mean (SD)**		**Mean (SD)**		
O1	5.72 (0.68)		5.66 (0.90)		
O2	5.66 (0.81)		5.94 (0.62)		
O3	5.75 (0.72)		5.92 (0.71)		
Change in Attitude Within Groups					**Between Groups**
	Control (N=28)		**Intervention (N=27)**		
Time	**Mean Difference (SE)**	**p-value [a]**	**Mean Difference (SE)**	**p-value [a]**	**p-value [a]**
O1-O2	-0.06 (0.11)	1.000	0.27 (0.11)	0.050	0.040*
O2-O3	0.09 (0.08)	0.820	-0.02 (0.08)	1.000	0.343
O1-O3	0.03 (0.10)	1.000	0.25 (0.10)	0.046*	0.128
Overall		0.552		0.036*	0.061
Attitudes Regarding Illicit Opioid Misuse					
Mean Attitude Scale Scores at O1, O2, O3					
	Control		**Intervention**		
Time	**Mean (SD)**		**Mean (SD)**		
O1	5.35 (0.99)		5.35 (1.06)		
O2	5.20 (1.15)		5.59 (0.95)		
O3	5.38 (0.96)		5.50 (0.97)		
Change in Attitude Within Groups					**Between Groups**
	Control (N=28)		**Intervention (N=27)**		
Time	**Mean Difference (SE)**	**p-value**	**Mean Difference (SE)**	**p-value [a]**	**p-value [a]**
O1-O2	-0.15 (0.15)	0.969	0.24 (0.15)	0.349	0.072
O2-O3	0.18 (0.14)	0.625	-0.08 (0.14)	1.000	0.195
O1-O3	0.03 (0.14)	1.000	0.16 (0.14)	0.825	0.531
Overall		0.425		0.283	0.157
Attitudes Regarding Prescription Opioid Misuse					
Mean Attitude Scale Scores at O1, O2, O3					
	Control		**Intervention**		
Time	**Mean (SD)**		**Mean (SD)**		
O1	5.90 (0.69)		5.82 (0.88)		
O2	5.82 (0.88)		6.11 (0.57)		
O3	5.93 (0.68)		6.12 (0.69)		
Change in Attitude Within Groups					**Between Groups**
	Control (N=28)		**Intervention (N=27)**		
Time	**Mean Difference (SE)**	**p-value**	**Mean Difference (SE)**	**p-value [a]**	**p-value [a]**
O1-O2	-0.01 (0.12)	1.000	0.29 (0.12)	0.057	0.082
O2-O3	0.04 (0.08)	1.000	0.01 (0.08)	1.000	0.779
O1-O3	0.03 (0.11)	1.000	0.30 (0.11)	0.022*	0.084
Overall		0.856		0.025*	0.094

Significance at the 0.05 level indicated by *.
[a] Based on results of mixed ANOVA with Bonferroni post-hoc tests.
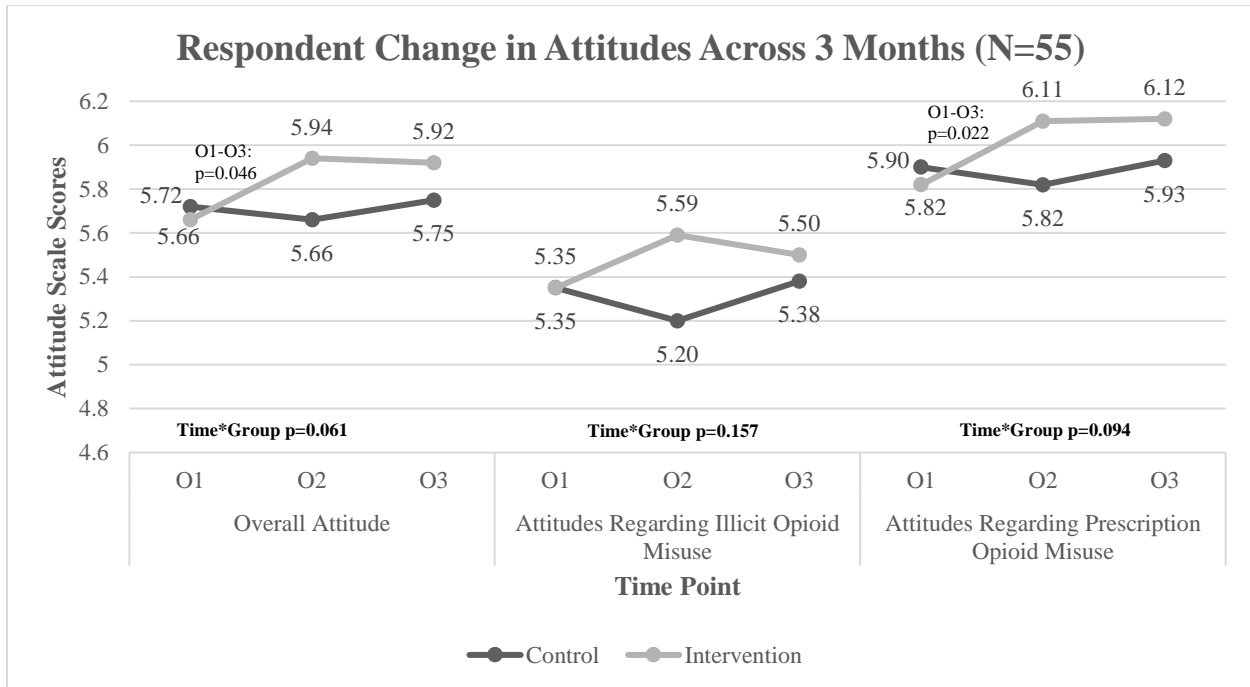
Figure 4.7 Change in Mean Attitude Scale Scores Over 3-Month Study Period. Only statistically significant p-values within groups are shown.

Confidence

The overall confidence scale had high internal consistency (Cronbach's alpha=0.895). Exploratory factor analysis (EFA) showed that confidence in providing pharmacy-based naloxone services was composed of 2 factors with eigenvalues >1: Confidence Regarding Patient-Oriented Activities (Cronbach's alpha=0.915); and Confidence Regarding Business-Oriented Activities (Cronbach's alpha=0.815) (see Appendix I). Respondent confidence at each time point is described below in terms of frequency of agreement or disagreement to scale items (Table 4.28).

Table 4.28 Confidence in Performing Pharmacy-Based Naloxone Services at O1, O2, O3

Question [a] *"I am confident in my ability to…"*	n (%) [b]					
	O1 (N=64)		O2 (N=62)		O3 (N=60)	
	C (N=32)	I (N=32)	C (N=30)	I (N=32)	C (N=30)	I (N=30)
Confidence Regarding Patient-Oriented Activities						
Proactively identify patients who would benefit from naloxone						
Strongly disagree	0	1 (3.1)	0	0	0	0
Disagree	1 (3.1)	0	0	0	0	1 (3.3)
Somewhat disagree	3 (0.4)	2 (6.3)	2 (6.9)	0	1 (3.3)	0
Neither agree nor disagree	2 (6.3)	2 (6.3)	0	3 (9.4)	1 (3.3)	1 (3.3)
Somewhat agree	9 (28.1)	**11 (34.4)**	7 (23.3)	4 (12.5)	8 (26.7)	6 (20.0)
Agree	**11 (34.4)**	9 (28.1)	**14 (48.3)**	**17 (53.1)**	**14 (46.7)**	**14 (46.7)**
Strongly agree	6 (18.8)	7 (21.9)	6 (20.7)	8 (25.0)	6 (20.0)	8 (26.7)
Communicate with physicians or other providers regarding their patients who may benefit from naloxone						
Strongly disagree	0	1 (3.1)	0	0	0	0
Disagree	1 (3.1)	0	1 (3.3)	0	0	0
Somewhat disagree	3 (9.4)	2 (6.3)	0	2 (6.3)	0	1 (3.3)
Neither agree nor disagree	1 (3.1)	3 (9.4)	0	1 (3.1)	1 (3.3)	2 (6.7)
Somewhat agree	6 (18.8)	**11 (34.4)**	6 (20.7)	4 (12.5)	7 (23.3)	5 (16.7)
Agree	**13 (40.6)**	8 (25.0)	**15 (51.7)**	**15 (46.9)**	**15 (50.0)**	**12 (40.0)**
Strongly agree	8 (25.0)	7 (21.9)	7 (24.1)	10 (31.3)	7 (23.3)	10 (33.3)
Initiate a conversation with a patient regarding the need for take-home naloxone						
Strongly disagree	0	1 (3.1)	0	0	0	0
Disagree	2 (6.3)	1 (3.1)	0	0	1 (3.3)	0
Somewhat disagree	3 (9.4)	3 (9.4)	5 (16.7)	0	1 (3.3)	0
Neither agree nor disagree	1 (3.1)	2 (6.3)	0	2 (6.3)	2 (6.7)	1 (3.3)
Somewhat agree	7 (21.9)	8 (25.0)	6 (20.7)	6 (18.8)	8 (26.7)	5 (16.7)
Agree	**14 (43.8)**	**12 (37.5)**	**13 (44.8)**	**16 (50.0)**	**13 (43.3)**	**17 (56.7)**
Strongly agree	5 (15.6)	5 (15.6)	5 (17.2)	8 (25.0)	5 (16.7)	7 (23.3)
Educate patients to recognize opioid overdose						
Strongly disagree	0	1 (3.1)	0	0	0	0

Disagree	1 (3.1)	1 (3.1)	0	0	0	0
Somewhat disagree	2 (6.3)	2 (6.3)	2 (6.9)	0	0	0
Neither agree nor disagree	1 (3.1)	1 (3.1)	0	0	1 (3.3)	2 (6.7)
Somewhat agree	5 (15.6)	9 (28.1)	6 (6.9)	6 (18.8)	8 (26.7)	4 (13.3)
Agree	**15 (46.9)**	**12 (37.5)**	**13 (44.8)**	**17 (53.1)**	**14 (46.7)**	**17 (56.7)**
Strongly agree	8 (25.0)	6 (18.8)	8 (27.6)	9 (28.1)	7 (23.3)	7 (23.3)
Counsel patients on how to safely administer naloxone when indicated						
Strongly disagree	1 (3.1)	1 (3.1)	0	0	0	0
Disagree	1 (3.1)	1 (3.1)	0	0	0	0
Somewhat disagree	1 (3.1)	1 (3.1)	1 (3.4)	0	0	0
Neither agree nor disagree	0	2 (6.3)	2 (6.9)	0	1 (3.3)	0
Somewhat agree	5 (15.6)	**10 (31.3)**	3 (10.3)	6 (18.8)	8 (26.7)	4 (13.3)
Agree	**17 (53.1)**	8 (25.0)	**14 (48.3)**	**15 (46.9)**	**14 (46.7)**	**17 (56.7)**
Strongly agree	7 (21.9)	9 (28.1)	9 (31.0)	11 (34.4)	7 (23.3)	9 (30.0)
Confidence Regarding Business-Oriented Activities						
Discuss naloxone cost with patients						
Strongly disagree	4 (12.5)	0	0	0	0	0
Disagree	0	0	0	0	0	1 (3.3
Somewhat disagree	0	2 (6.3)	1 (3.4)	0	0	0
Neither agree nor disagree	2 (6.3)	1 (3.1)	3 (10.3)	0	2 (6.7)	0
Somewhat agree	3 (9.4)	7 (21.9)	3 (10.3)	4 (12.5)	5 (16.7)	3 (10.0)
Agree	**15 (46.9)**	**13 (40.6)**	**14 (48.3)**	**18 (56.3)**	**14 (46.7)**	**16 (53.3)**
Strongly agree	8 (25.0)	9 (28.1)	8 (27.6)	10 (31.3)	9 (30.0)	10 (33.3)
Stock naloxone products in my pharmacy						
Strongly disagree	0	0	0	0	0	0
Disagree	0	0	1 (3.4)	2 (6.3)	1 (3.3)	1 (3.3)
Somewhat disagree	0	3 (9.4)	1 (3.4)	0	0	0
Neither agree nor disagree	1 (3.1)	2 (6.3)	2 (6.9)	0	2 (6.7)	4 (13.3)
Somewhat agree	1 (3.1)	5 (15.6)	2 (6.9)	4 (12.5)	1 (3.3)	2 (6.7)
Agree	**16 (50.0)**	9 (28.1)	11 (37.9)	9 (28.1)	**16 (53.3)**	9 (30.0)
Strongly agree	14 (43.8)	**13 (40.6)**	**12 (41.4)**	**17 (53.1)**	10 (33.3)	**14 (46.7)**
Dispense naloxone products in my pharmacy when prescribed by a physician						
Strongly disagree	0	0	0	0	0	0
Disagree	0	0	0	1 (3.1)	0	1 (3.3)

Somewhat disagree	0	0	0	0	0	0
Neither agree nor disagree	0	1 (3.1)	0	1 (3.1)	0	1 (3.3)
Somewhat agree	0	4 (12.5)	0	1 (3.1)	1 (3.3)	5 (16.7)
Agree	15 (46.9)	8 (25.0)	**13 (44.8)**	10 (31.3)	**15 (50.0)**	5 (16.7)
Strongly agree	**17 (53.1)**	**19 (59.4)**	16 (55.2)	**19 (59.4)**	14 (46.7)	**18 (60.0)**
Dispense naloxone products in my pharmacy using Alabama's statewide standing order						
Strongly disagree	0	0	0	0	1 (3.3)	0
Disagree	2 (6.3)	0	0	1 (3.1)	1 (3.3)	1 (3.3)
Somewhat disagree	2 (6.3)	1 (3.1)	4 (13.8)	0	2 (6.7)	0
Neither agree nor disagree	4 (12.5)	2 (6.3)	3 (10.3)	2 (6.3)	7 (23.3)	3 (10.0)
Somewhat agree	5 (15.6)	9 (28.1)	4 (13.8)	3 (9.4)	1 (3.3)	4 (13.3)
Agree	**11 (34.4)**	**11 (34.4)**	12 (41.4)	13 (40.6)	13 (43.3)	11 (36.7)
Strongly agree	8 (25.0)	9 (28.1)	6 (20.7)	**13 (40.6)**	5 (16.7)	**11 (36.7)**
Correctly bill insurance companies for dispensed naloxone products						
Strongly disagree	1 (3.1)	0	0	0	0	0
Disagree	0	1 (3.1)	0	0	0	0
Somewhat disagree	0	4 (12.5)	0	1 (3.1)	0	0
Neither agree nor disagree	1 (3.1)	5 (15.6)	2 (6.9)	5 (15.6)	2 (6.7)	2 (6.7)
Somewhat agree	5 (15.6)	2 (6.3)	4 (13.8)	2 (6.3)	1 (3.3)	2 (6.7)
Agree	**15 (46.9)**	9 (28.1)	11 (37.9)	10 (31.3)	**16 (53.3)**	10 (33.3)
Strongly agree	10 (31.3)	**11 (34.4)**	**12 (41.4)**	**14 (43.8)**	11 (36.7)	**16 (53.3)**

C=Control group, I=Intervention group

[a] On a Likert-type scale of 1 to 7, where 1=strongly disagree and 7=strongly agree.

[b] Percentages may differ due to item non-response.

Higher mean scale scores represent greater confidence. Among the 55 individuals who responded to all 3 surveys, the mean overall confidence scale score was above 5.00 for both groups at each time point (Tables 4.29a-b). Specifically, the mean (SD) overall confidence scale score among the intervention group was 5.52 (1.03) at O1, 6.16 (0.74) at O2, and 6.12 (0.75) O3. Among the control group, mean (SD) overall confidence scores were 5.75 (0.83) at O1, 5.85 (0.70) at O2, and 5.86 (0.57) at O3. Similar patterns for were seen for confidence regarding patient-oriented activities and confidence regarding business-oriented activities, with mean scale scores for confidence towards patient-oriented activities being generally lower and confidence towards business-oriented activities being generally higher.

Changes in mean overall confidence scale scores across O1, O2, and O3 were also assessed for the 55 individuals who responded to all 3 surveys (Tables 4.29a-b, Figure 4.8). Values are mean (SD) unless stated otherwise. There was a statistically significant increase in overall confidence scale score within the intervention group from O1 to O2 (5.52 to 6.16, $p<0.0005$), and this change was maintained at 3 months (O2-O3: -0.04, $p=1.000$). The change within the intervention group was statistically significant compared to control ($p=0.008$).

Furthermore, for confidence regarding patient-oriented versus business-oriented activities, confidence tended to be lower for the patient-oriented category compared to the business-oriented category in each group. For confidence regarding patient-oriented activities, there was a statistically significant increase in the scale score within the intervention group from O1 to O2 (5.52 to 6.16, $p=0.001$), and this change was maintained at 3 months (O2-O3: -0.22, $p=1.000$). The change within the intervention group was statistically significant compared to control ($p=0.047$). Additionally, there was a statistically significant increase in the confidence regarding business-oriented activities scale score within the intervention group from O1 to O2

207

(5.79 to 6.25, p=0.002), and this change was maintained at 3 months (O2-O3: -0.06, p=1.000). The change within the intervention group was statistically significant compared to control (p=0.012). Overall, when compared to control, the training program affected pharmacists' overall confidence towards pharmacy-based naloxone services (p=0.016) as well as confidence regarding patient-oriented activities (p=0.029), but not confidence regarding business-oriented activities (p=0.060) over 3 months.

In summary, hypothesis 4a stated that change in confidence regarding naloxone services from baseline to post-training and baseline to 3-months will be greater among intervention compared to control group pharmacists. We rejected the null hypothesis, and concluded that the training program had an effect on pharmacist confidence overall.

Table 4.29a. Overall Effect of the Intervention on Confidence

Overall Confidence		
Factor	**F**	**p-value [a]**
Time	8.657	<0.0005*
Time * Group	4.460	0.016*
Group	0.400	0.530
Confidence Regarding Patient-Oriented Activities		
Time	9.447	<0.0005*
Time * Group	3.044	0.060
Group	0.199	0.657
Confidence Regarding Business-Oriented Activities		
Time	3.123	0.048*
Time * Group	3.676	0.029*
Group	0.469	0.497

Table 4.29b. Change in Mean Confidence Scale Score in Control and Intervention Groups Over 3 Months (N=55)

	Overall Confidence				
	Mean Confidence Scale Scores at O1, O2, O3				
	Control		**Intervention**		
Time	**Mean (SD)**		**Mean (SD)**		
O1	5.75 (0.83)		5.52 (1.03)		
O2	5.85 (0.70)		6.16 (0.74)		
O3	5.86 (0.57)		6.12 (0.75)		
	Change in Confidence Within Groups				**Between Groups**
	Control (N=28)		**Intervention (N=27)**		
Time	**Mean Difference (SE)**	**p-value [a]**	**Mean Difference (SE)**	**p-value [a]**	**p-value [a]**
O1-O2	0.10 (0.14)	1.000	0.64 (0.14)	<0.0005*	0.008*
O2-O3	0.004 (0.12)	1.000	-0.04 (0.12)	1.000	0.793
O1-O3	0.10 (0.16)	1.000	0.60 (0.16)	0.002*	0.037*
Overall		0.760		<0.0005*	0.016*
	Confidence Regarding Patient-Oriented Activities				
	Mean Confidence Scale Scores at O1, O2, O3				
	Control		**Intervention**		
Time	**Mean (SD)**		**Mean (SD)**		
O1	5.55 (1.15)		5.25 (1.32)		
O2	5.76 (0.90)		6.07 (0.73)		
O3	5.78 (0.73)		6.04 (0.68)		
	Change in Confidence Within Groups				**Between Groups**
	Control (N=28)		**Intervention (N=27)**		
Time	**Mean Difference (SE)**	**p-value [a]**	**Mean Difference (SE)**	**p-value [a]**	**p-value [a]**
O1-O2	0.22 (0.21)	0.926	0.82 (0.21)	0.001*	0.047*
O2-O3	0.015 (0.14)	1.000	-0.22 (0.14)	1.000	0.854
O1-O3	0.23 (0.22)	0.892	0.79 (0.22)	0.002*	0.074
Overall		0.554		0.001*	0.060
	Confidence Regarding Business-Oriented Activities				
	Mean Confidence Scale Scores at O1, O2, O3				
	Control		**Intervention**		
Time	**Mean (SD)**		**Mean (SD)**		
O1	5.96 (0.80)		5.79 (0.99)		
O2	5.94 (0.73)		6.25 (0.88)		
O3	5.93 (0.60)		6.19 (0.93)		
	Change in Confidence Within Groups				**Between Groups**
	Control (N=28)		**Intervention (N=27)**		
Time	**Mean Difference (SE)**	**p-value**	**Mean Difference (SE)**	**p-value [a]**	**p-value [a]**
O1-O2	-0.02 (0.13)	1.000	0.46 (0.13)	0.002*	0.012*
O2-O3	-0.01 (0.13)	1.000	-0.06 (0.13)	1.000	0.779
O1-O3	-0.02 (0.15)	1.000	0.40 (0.15)	0.027*	0.048*
Overall		0.988		0.003*	0.029*

Significance at the 0.05 level indicated by *.

[a] Based on results of mixed ANOVA with Bonferroni post-hoc tests.
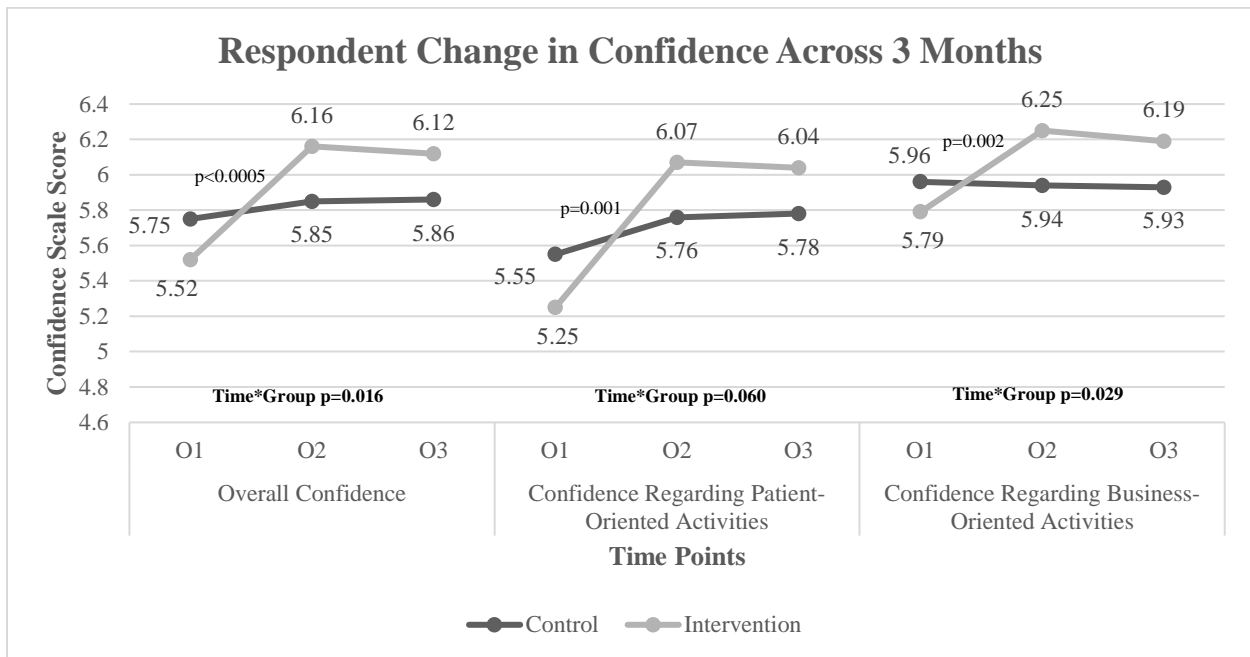
Figure 4.8 Change in Mean Confidence Scale Scores Over 3-Month Study Period. Only statistically significant p-values within groups are shown.

Perceived Barriers

The overall perceived barriers scale had high internal consistency (Cronbach's alpha=0.891). Exploratory factor analysis (EFA) showed that perceived barriers to implementing pharmacy-based naloxone services was composed of 2 factors with eigenvalues >1: Barriers Related to Support and Resources (Cronbach's alpha=0.890); and Barriers Related to Business Logistics (Cronbach's alpha=0.802) (see Appendix J). Respondents' perceived barriers at each time point are described below in terms of frequency of agreement or disagreement to scale items (Table 4.30).

Table 4.30 Perceived Barriers to Pharmacy-Based Naloxone Services at O1, O2, O3

Question [a]	n (%) [b]					
	O1 (N=64)		O2 (N=62)		O3 (N=60)	
	C (N=32)	I (N=32)	C (N=30)	I (N=32)	C (N=30)	I (N=30)
Barriers Related to Support and Resources						
The level of general support from management, corporate, or owners is low						
Strongly disagree	7 (21.9)	**13 (40.6)**	5 (17.2)	**12 (37.5)**	7 (23.3)	**11 (36.7)**
Disagree	**10 (31.3)**	7 (21.9)	**8 (27.6)**	3 (9.4)	**8 (26.7)**	**11 (36.7)**
Somewhat disagree	3 (9.4)	3 (9.4)	6 (20.7)	2 (6.3)	2 (6.7)	0
Neither agree nor disagree	4 (12.5)	2 (6.3)	5 (17.2)	8 (25.0)	7 (23.3)	3 (10.0)
Somewhat agree	4 (12.5)	3 (9.4)	2 (6.9)	4 (12.5)	3 (10.0)	5 (16.7)
Agree	4 (12.5)	3 (9.4)	2 (6.9)	2 (6.3)	3 (10.0)	0
Strongly agree	0	1 (3.1)	1 (3.4)	1 (3.1)	0	0
The level of general support from other pharmacists for naloxone services is low						
Strongly disagree	3 (9.4)	8 (25.0)	3 (10.3)	**10 (31.3)**	5 (16.7)	8 (26.7)
Disagree	**9 (28.1)**	8 (25.0)	**7 (24.1)**	5 (15.6)	**9 (30.0)**	**10 (33.3)**
Somewhat disagree	5 (15.6)	1 (3.1)	**7 (24.1)**	5 (15.6)	3 (10.0)	2 (6.7)
Neither agree nor disagree	6 (18.8)	**9 (28.1)**	4 (13.8)	5 (15.6)	5 (16.7)	6 (20.0)
Somewhat agree	3 (9.4)	6 (18.8)	5 (17.2)	7 (21.9)	6 (20.0)	4 (13.3)
Agree	6 (18.8)	0	2 (6.9)	0	2 (6.7)	0
Strongly agree	0	0	1 (3.4)	0	0	0
The level of general support from technicians for naloxone services is low						
Strongly disagree	3 (9.4)	**11 (34.4)**	3 (10.0)	**9 (28.1)**	5 (16.7)	**10 (33.3)**
Disagree	**11 (34.4)**	6 (18.8)	**8 (27.6)**	8 (25.0)	**8 (26.7)**	8 (26.7)
Somewhat disagree	3 (9.4)	3 (9.4)	0	3 (9.4)	4 (13.3)	2 (6.7)
Neither agree nor disagree	5 (15.6)	7 (21.9)	7 (24.1)	6 (18.8)	5 (16.7)	5 (16.7)
Somewhat agree	2 (6.3)	5 (15.6)	4 (13.8)	6 (18.8)	3 (10.0)	5 (16.7)
Agree	6 (18.8)	0	4 (13.8)	0	3 (10.0)	0
Strongly agree	2 (6.3)	0	3 (10.3)	0	2 (6.7)	0
The level of general support from local physicians is low						
Strongly disagree	1 (3.1)	4 (12.5)	2 (6.9)	3 (9.4)	3 (10.0)	4 (13.3)
Disagree	**12 (37.5)**	6 (18.8)	7 (24.1)	5 (15.6)	6 (20.0)	**8 (26.7)**

Somewhat disagree	2 (6.3)	3 (9.4)	3 (10.3)	2 (6.3)	3 (10.0)	3 (10.0)
Neither agree nor disagree	6 (18.8)	**8 (25.0)**	**8 (27.6)**	**10 (31.3)**	**8 (26.7)**	6 (20.0)
Somewhat agree	5 (15.6)	5 (15.6)	4 (13.8)	8 (25.0)	**8 (26.7)**	7 (23.3)
Agree	6 (18.8)	4 (12.5)	4 (13.8)	3 (9.4)	1 (3.3)	0
Strongly agree	0	2 (6.3)	1 (3.4)	1 (3.1)	1 (3.3)	2 (6.7)
I am unfamiliar with my state's laws and regulations about naloxone						
Strongly disagree	3 (9.4)	9 (28.1)	3 (10.3)	9 (28.1)	6 (20.0)	10 (3.3)
Disagree	**12 (37.5)**	**10 (31.3)**	**9 (31.0)**	**14 (43.8)**	**14 (46.7)**	**9 (30.0)**
Somewhat disagree	2 (6.3)	4 (12.5)	5 (17.2)	4 (12.5)	4 (13.3)	2 (6.7)
Neither agree nor disagree	4 (12.5)	1 (3.1)	1 (3.4)	2 (6.3)	2 (6.7)	4 (13.3)
Somewhat agree	8 (25.0)	5 (15.6)	8 (27.6)	1 (3.1)	3 (10.0)	2 (6.7)
Agree	0	3 (9.4)	3 (10.3)	2 (6.3)	1 (3.3)	3 (10.0)
Strongly agree	3 (9.4)	0	0	0	0	0
Pharmacy technician staff are not sufficiently trained to implement naloxone services						
Strongly disagree	0	3 (9.4)	0	2 (6.3)	3 (10.0)	5 (16.7)
Disagree	5 (15.6)	1 (3.1)	3 (10.3)	3 (9.4)	4 (13.3)	4 (13.3)
Somewhat disagree	5 (15.6)	0	2 (6.9)	3 (9.4)	4 (13.3)	2 (6.7)
Neither agree nor disagree	2 (6.3)	3 (9.4)	3 (10.3)	5 (15.6)	3 (10.0)	2 (6.7)
Somewhat agree	3 (9.4)	7 (21.9)	9 (31.0)	**9 (28.1)**	4 (13.3)	**9 (30.0)**
Agree	8 (25.0)	**13 (40.6)**	**10 (34.5)**	4 (12.5)	**10 (33.3)**	7 (23.3)
Strongly agree	**9 (28.1)**	5 (15.6)	2 (6.9)	6 (18.8)	2 (6.7)	1 (3.3)
Dispensing naloxone is too time-consuming						
Strongly disagree	4 (12.5)	7 (21.9)	4 (13.8)	6 (18.8)	6 (20.0)	4 (13.3)
Disagree	4 (12.5)	**8 (25.0)**	**7 (24.1)**	6 (18.8)	**8 (26.7)**	**8 (26.7)**
Somewhat disagree	6 (18.8)	3 (9.4)	3 (10.3)	3 (9.4)	4 (13.3)	5 (16.7)
Neither agree nor disagree	**11 (34.4)**	**8 (25.0)**	**7 (24.1)**	8 (25.0)	7 (23.3)	7 (23.3)
Somewhat agree	4 (12.5)	5 (15.6)	6 (20.7)	**9 (28.1)**	3 (10.0)	5 (16.7)
Agree	3 (9.4)	1 (3.1)	2 (6.9)	0	0	1 (3.3)
Strongly agree	0	0	0	0	2 (6.7)	0
Counseling patients about naloxone is too time-consuming						
Strongly disagree	5 (15.6)	**8 (25.0)**	6 (20.7)	6 (18.8)	7 (23.3)	5 (16.7)
Disagree	**12 (37.5)**	**8 (25.0)**	**10 (34.5)**	**9 (28.1)**	11 (36.7)	10 (33.3)
Somewhat disagree	5 (15.6)	6 (18.8)	5 (17.2)	3 (9.4)	5 (16.7)	6 (20.0)
Neither agree nor disagree	4 (12.5)	4 (12.5)	2 (6.9)	3 (9.4)	3 (10.0)	5 (16.7)

Somewhat agree	2 (6.3)	6 (18.8)	4 (13.8)	**9 (28.1)**	2 (6.7)	4 (13.3)
Agree	4 (12.5)	0	2 (6.9)	1 (3.1)	0	0
Strongly agree	0	0	0	1 (3.1)	2 (6.7)	0
There are not enough pharmacy staff members						
Strongly disagree	1 (3.1)	5 (15.6)	2 (6.9)	4 (12.5)	4 (13.3)	3 (10.0)
Disagree	**11 (34.4)**	6 (18.8)	**8 (27.6)**	4 (12.5)	3 (13.3)	6 (20.0)
Somewhat disagree	2 (6.3)	2 (6.3)	2 (6.9)	3 (9.4)	**6 (20.0)**	3 (10.0)
Neither agree nor disagree	4 (12.5)	5 (15.6)	6 (20.7)	4 (12.5)	3 (10.0)	3 (10.0)
Somewhat agree	4 (12.5)	5 (15.6)	5 (17.2)	**8 (25.0)**	5 (16.7)	**8 (26.7)**
Agree	6 (18.8)	**7 (21.9)**	4 (13.8)	4 (12.5)	4 (13.3)	2 (6.7)
Strongly agree	4 (12.5)	2 (6.3)	2 (6.9)	5 (15.6)	4 (13.3)	5 (16.7)
It is difficult to identify patients who would benefit from naloxone						
Strongly disagree	3 (9.4)	2 (6.3)	3 (10.3)	5 (15.6)	3 (10.0)	2 (6.7)
Disagree	11 (34.4)	**11 (34.4)**	**9 (31.0)**	**13 (40.6)**	**11 (36.7)**	**14 (46.7)**
Somewhat disagree	4 (12.5)	5 (15.6)	**9 (31.0)**	8 (25.0)	6 (20.0)	6 (20.0)
Neither agree nor disagree	1 (3.1)	4 (12.5)	4 (13.8)	4 (12.5)	2 (6.7)	3 (10.0)
Somewhat agree	**12 (37.5)**	7 (21.9)	3 (10.3)	2 (6.3)	6 (20.0)	4 (13.3)
Agree	0	2 (6.3)	1 (3.4)	0	1 (3.3)	1 (3.3)
Strongly agree	1 (3.1)	1 (3.1)	0	0	1 (3.3)	0
There are concerns over clientele who might frequent the pharmacy if naloxone services were in place						
Strongly disagree	3 (9.4)	6 (18.8)	2 (6.9)	3 (9.4)	5 (16.7)	4 (13.3)
Disagree	**7 (21.9)**	**9 (28.1)**	8 (27.6)	**11 (34.4)**	7 (23.3)	**10 (33.3)**
Somewhat disagree	6 (18.8)	3 (9.4)	5 (17.2)	4 (12.5)	4 (13.3)	4 (13.3)
Neither agree nor disagree	6 (18.8)	7 (21.9)	**9 (31.0)**	8 (25.0)	6 (20.0)	7 (23.3)
Somewhat agree	5 (15.6)	5 (15.6)	2 (6.9)	6 (18.8)	6 (20.0)	5 (16.7)
Agree	3 (9.3)	1 (3.1)	3 (10.3)	0	2 (6.7)	0
Strongly agree	2 (6.3)	1 (3.1)	0	0	0	0
There are moral or ethical concerns associated with increasing drug abuse as a result of providing naloxone						
Strongly disagree	6 (18.8)	**10 (31.3)**	3 (10.3)	5 (15.6)	**9 (30.0)**	6 (20.0)
Disagree	**9 (28.1)**	8 (25.0)	**12 (41.4)**	**11 (34.4)**	8 (26.7)	**10 (33.3)**
Somewhat disagree	3 (9.4)	5 (15.6)	7 (24.1)	5 (15.6)	2 (6.7)	1 (3.3)
Neither agree nor disagree	5 (15.6)	3 (9.4)	3 (10.3)	7 (21.9)	7 (23.3)	7 (23.3)
Somewhat agree	6 (18.8)	5 (15.6)	2 (6.9)	2 (6.3)	3 (10.0)	4 (13.3)

213

Agree	1 (3.1)	1 (3.1)	2 (6.9)	1 (3.1)	0	2 (6.7)
Strongly agree	2 (6.3)	0	0	1 (3.1)	1 (3.3)	0
There is community opposition to providing naloxone						
Strongly disagree	4 (12.5)	4 (12.5)	5 (17.2)	3 (9.4)	5 (16.7)	6 (20.0)
Disagree	**15 (46.9)**	9 (28.1)	**10 (34.5)**	**13 (40.6)**	**11 (36.7)**	**11 (36.7)**
Somewhat disagree	6 (18.8)	4 (12.5)	3 (10.3)	6 (18.8)	3 (10.0)	4 (13.3)
Neither agree nor disagree	7 (21.9)	**11 (34.4)**	8 (27.6)	7 (21.9)	9 (30.0)	5 (16.7)
Somewhat agree	0	3 (9.4)	3 (10.3)	2 (6.3)	2 (6.7)	4 (13.3)
Agree	0	0	0	0	0	0
Strongly agree	0	1 (3.1)	0	1 (3.1)	0	0
Barriers Related to Business Logistics						
It is difficult to package or stock the various forms of naloxone						
Strongly disagree						
Disagree	4 (12.5)	5 (15.6)	3 (10.3)	**7 (21.9)**	4 (13.3)	7 (23.3)
Somewhat disagree	**12 (37.5)**	5 (15.6)	8 (27.6)	**7 (21.9)**	**11 (36.7)**	**11 (36.7)**
Neither agree nor disagree	4 (12.5)	1 (3.1)	4 (13.8)	3 (9.4)	4 (13.3)	1 (3.3)
Somewhat agree	2 (6.3)	**10 (31.3)**	**10 (34.5)**	4 (12.5)	4 (13.3)	2 (6.7)
Agree	4 (12.5)	4 (12.5)	3 (10.3)	**7 (21.9)**	1 (3.3)	5 (16.7)
Strongly agree	6 (18.8)	4 (12.5)	0	1 (3.10)	**5 (16.7)**	4 (13.3)
	0	3 (9.4)	1 (3.4)	3 (9.4)	1 (3.3)	0
Naloxone expiration dates are too short						
Strongly disagree	2 (6.3)	2 (6.3)	0	1 (3.1)	1 (3.3)	2 (6.7)
Disagree	2 (6.3)	3 (9.4)	4 (13.8)	5 (15.6)	5 (16.7)	7 (23.3)
Somewhat disagree	4 (12.5)	0	3 (10.3)	1 (3.1)	3 (10.0)	1 (3.3)
Neither agree nor disagree	**18 (56.3)**	**18 (56.3)**	**16 (55.2)**	**16 (50.0)**	**18 (60.0)**	**9 (30.0)**
Somewhat agree	4 (12.5)	7 (21.9)	4 (13.8)	8 (25.0)	0	7 (23.3)
Agree	2 (6.3)	1 (3.1)	0	1 (3.1)	2 (6.7)	4 (13.3)
Strongly agree	0	1 (3.1)	2 (6.9)	0	1 (3.3)	0
The cost of stocking naloxone is too high						
Strongly disagree	3 (9.4)	3 (9.4)	2 (6.9)	4 (12.5)	3 (10.0)	3 (10.0)
Disagree	7 (21.9)	2 (6.3)	**8 (27.6)**	5 (15.6)	5 (16.7)	**7 (23.3)**
Somewhat disagree	1 (3.1)	2 (6.3)	3 (10.3)	2 (6.3)	5 (16.7)	2 (6.7)
Neither agree nor disagree	**8 (25.0)**	**10 (31.3)**	8 (27.6)	7 (21.9)	**8 (26.7)**	**7 (23.3)**
Somewhat agree	**8 (25.0)**	**10 (31.3)**	3 (10.3)	**9 (28.1)**	4 (13.3)	6 (20.0)
Agree	4 (12.5)	0	3 (10.3)	2 (6.3)	3 (13.3)	4 (13.3)
Strongly agree	1 (3.1)	5 (15.6)	2 (6.9)	3 (9.4)	2 (6.7)	1 (3.3)

It is difficult to obtain reimbursement from third-party payers						
Strongly disagree	2 (6.3)	2 (6.3)	1 (3.4)	2 (6.3)	0	2 (6.7)
Disagree	6 (18.8)	4 (12.5)	5 (17.2)	5 (15.6)	7 (23.3)	7 (23.3)
Somewhat disagree	2 (6.3)	1 (3.1)	1 (3.4)	1 (3.1)	3 (10.0)	1 (3.3)
Neither agree nor disagree	**16 (50.0)**	**13 (40.6)**	**13 (44.8)**	**10 (31.3)**	**11 (36.7)**	**9 (30.0)**
Somewhat agree	2 (6.3)	4 (12.5)	5 (17.2)	7 (21.9)	4 (13.3)	6 (20.0)
Agree	3 (9.4)	1 (3.1)	3 (10.3)	5 (15.6)	4 (13.3)	3 (10.0)
Strongly agree	1 (3.1)	7 (21.9)	1 (3.4)	2 (6.3)	1 (3.3)	2 (6.7)
The amount patients have to pay for naloxone is too high						
Strongly disagree	2 (6.3)	0	3 (10.3)	2 (6.3)	0	1 (3.3)
Disagree	3 (9.4)	4 (12.5)	1 (3.4)	3 (9.4)	4 (13.3)	7 (23.3)
Somewhat disagree	2 (6.3)	4 (12.5)	2 (6.9)	1 (3.1)	4 (13.3)	6 (20.0)
Neither agree nor disagree	**12 (37.5)**	**7 (21.9)**	7 (24.1)	5 (15.6)	7 (23.3)	6 (20.0)
Somewhat agree	7 (21.9)	**7 (21.9)**	**8 (27.6)**	**12 (37.5)**	**8 (26.7)**	**12 (40.0)**
Agree	4 (12.5)	3 (9.4)	6 (20.7)	2 (6.3)	3 (10.0)	1 (3.3)
Strongly agree	2 (6.3)	**7 (21.9)**	2 (6.9)	7 (21.9)	4 (13.3)	3 (10.0)
There is not enough profit margin						
Strongly disagree	1 (3.1)	3 (9.4)	2 (6.9)	3 (9.4)	2 (6.7)	2 (6.7)
Disagree	2 (6.3)	0	4 (13.8)	3 (9.4)	5 (16.7)	7 (23.3)
Somewhat disagree	1 (3.1)	0	0	4 (12.5)	2 (6.7)	1 (3.3)
Neither agree nor disagree	**20 (62.5)**	**20 (62.5)**	**22 (75.9)**	**14 (43.8)**	**17 (56.7)**	**9 (30.0)**
Somewhat agree	2 (6.3)	4 (12.5)	0	3 (9.4)	1 (3.3)	7 (23.3)
Agree	4 (12.5)	1 (3.1)	1 (3.4)	2 (6.3)	3 (10.0)	1 (3.3)
Strongly agree	2 (6.3)	4 (12.5)	0	3 (9.4)	0	3 (10.0)
Patients are not interested in receiving naloxone from the pharmacy						
Strongly disagree	1 (3.1)	2 (6.3)	1 (3.4)	1 (3.1)	2 (6.7)	0
Disagree	3 (9.4)	3 (9.4)	4 (13.8)	3 (9.4)	3 (10.0)	4 (13.3)
Somewhat disagree	3 (9.4)	2 (6.3)	5 (17.2)	5 (15.6)	2 (6.7)	1 (3.3)
Neither agree nor disagree	**11 (34.4)**	3 (9.4)	6 (20.7)	6 (18.8)	7 (23.3)	6 (20.0)
Somewhat agree	3 (9.4)	**11 (34.4)**	**7 (24.1)**	**7 (21.9)**	**11 (36.7)**	**13 (43.3)**
Agree	9 (28.1)	7 (21.9)	5 (17.2)	**7 (21.9)**	4 (13.3)	4 (13.3)
Strongly agree	2 (6.3)	4 (12.5)	1 (3.4)	3 (9.4)	1 (3.3)	2 (6.7)

C=Control group, I=Intervention group

[a] On a Likert-type scale of 1 to 7, where 1=strongly disagree and 7=strongly agree.

[b] Percentages may differ due to item non-response.

Higher mean values represent more perceived barriers, whereas lower mean values represent less perceived barriers. Among the 55 individuals who responded to all 3 surveys, the mean overall perceived barriers scale score was below 4.00 for both groups at each time point (Tables 4.31a-b). Specifically, the mean (SD) overall perceived barriers scale score among the intervention group was 3.67 (0.99) at O1, 3.53 (0.94) at O2, and 3.23 (0.90) O3. Among the control group, mean (SD) overall perceived barriers scores were 3.68 (0.94) at O1, 3.57 (0.93) at O2, and 3.40 (1.10) at O3. Similar patterns were seen for perceived barriers regarding support and resources and perceived barriers regarding business logistics, with mean scale scores for perceived barriers towards support and resources being generally lower and perceived barriers towards business logistics being generally higher.

Changes in mean perceived barriers scale scores across O1, O2, and O3 were also assessed for the 55 individuals who responded to all 3 surveys (Tables 4.31a-b, Figure 4.9). Values are mean (SD) unless stated otherwise. There was a statistically significant decrease in overall perceived barriers scale score within the intervention group from O1 to O3 (3.67 to 3.23, p=0.001) but not O1 to O2. However, this change was not statistically significant compared to control (p=0.337).

Furthermore, for perceived barriers related to support and resources versus business logistics, barriers tended to be lower for the support and resources category compared to the business logistics category in each group. For perceived barriers related to support and resources, there was a statistically significant decrease in the scale score within the intervention group from O1 to O3 (3.31 to 2.92, p=0.008) but not O1 to O2. However, this change was not statistically significant compared to control (p=0.883). Additionally, there was a statistically significant decrease in the perceived barriers related to business logistics scale score within the

intervention group from O1 to O2 (4.34 to 4.06, p=0.029), and this change was maintained at 3 months (O2-O3: -0.25, p=0.293). However, the change within the intervention group was not statistically significant compared to control (p=0.365). Overall, when compared to control, the training program did not affect pharmacists' perceived barriers towards pharmacy-based naloxone services overall (p=0.585), related to support and resources (p=0.971), or related to business logistics (p=0.128) over 3 months.

In summary, hypothesis 5a stated that change in perceived barriers regarding naloxone services from baseline to post-training and baseline to 3-months will be greater among intervention compared to control group pharmacists. We failed to reject the null hypothesis, and concluded that the training program had no effect on pharmacist perceived barriers overall.

Table 4.31a Overall Effect of the Intervention on Perceived Barriers

Overall Perceived Barriers		
Factor	**F**	**p-value [a]**
Time	11.220	<0.0005
Time * Group	0.539	0.585
Group	0.123	0.727
Barriers Related to Support and Resources		
Time	10.911	<0.0005
Time * Group	0.030	0.971
Group	0.604	0.441
Barriers Related to Business Logistics		
Time	5.825	0.004
Time * Group	2.155	0.128
Group	0.245	0.623

Table 4.31b Change in Mean Perceived Barriers Scale Score in Control and Intervention Groups Over 3 Months (N=55)

	Overall Perceived Barriers				
	Mean Perceived Barrier Scores at O1, O2, O3				
	Control			**Intervention**	
Time	**Mean (SD)**			**Mean (SD)**	
O1	3.68 (0.94)			3.67 (0.99)	
O2	3.57 (0.93)			3.53 (0.94)	
O3	3.40 (1.10)			3.23 (0.90)	
	Change in Perceived Barriers Within Groups				**Between Groups**
	Control (N=28)		**Intervention (N=27)**		
Time	**Mean Difference (SE)**	**p-value [a]**	**Mean Difference (SE)**	**p-value [a]**	**p-value [a]**
O1-O2	-0.11 (0.09)	0.756	-0.18 (0.09)	0.162	0.568
O2-O3	-0.18 (0.12)	0.410	-0.26 (0.12)	0.087	0.607
O1-O3	-0.28 (0.12)	0.057	-0.44 (0.12)	0.001*	0.337
Overall		0.64		0.002*	0.585

	Barriers Related to Support and Resources				
	Mean Perceived Barrier Scores at O1, O2, O3				
	Control			**Intervention**	
Time	**Mean (SD)**			**Mean (SD)**	
O1	3.50 (1.12)			3.31 (1.11)	
O2	3.42 (1.03)			3.19 (0.92)	
O3	3.14 (1.20)			2.92 (0.98)	
	Change in Perceived Barriers Within Groups				**Between Groups**
	Control (N=28)		**Intervention (N=27)**		
Time	**Mean Difference (SE)**	**p-value [a]**	**Mean Difference (SE)**	**p-value [a]**	**p-value [a]**
O1-O2	-0.08 (0.11)	1.000	-0.12 (0.11)	0.789	0.796
O2-O3	-0.28 (0.12)	0.074	-0.27 (0.12)	0.097	0.934
O1-O3	-0.36 (0.12)	0.014*	-0.39 (0.12)	0.008*	0.883
Overall		0.016*		0.011*	0.971

	Barriers Related to Business Logistics				
	Mean Perceived Barrier Scores at O1, O2, O3				
	Control			**Intervention**	
Time	**Mean (SD)**			**Mean (SD)**	
O1	4.02 (1.00)			4.34 (1.21)	
O2	3.87 (1.02)			4.06 (1.37)	
O3	3.88 (1.06)			3.80 (1.28)	
	Change in Perceived Barriers Within Groups				**Between Groups**
	Control (N=28)		**Intervention (N=27)**		
Time	**Mean Difference (SE)**	**p-value**	**Mean Difference (SE)**	**p-value [a]**	**p-value [a]**
O1-O2	-0.15 (0.11)	0.511	-0.286 (0.11)	0.029*	0.365
O2-O3	0.016 (0.15)	1.000	-0.25 (0.15)	0.293	0.211
O1-O3	-0.132 (0.16)	1.000	-0.540 (0.16)	0.004*	0.078
Overall		0.381		0.003*	0.128

Significance at the 0.05 level indicated by *.
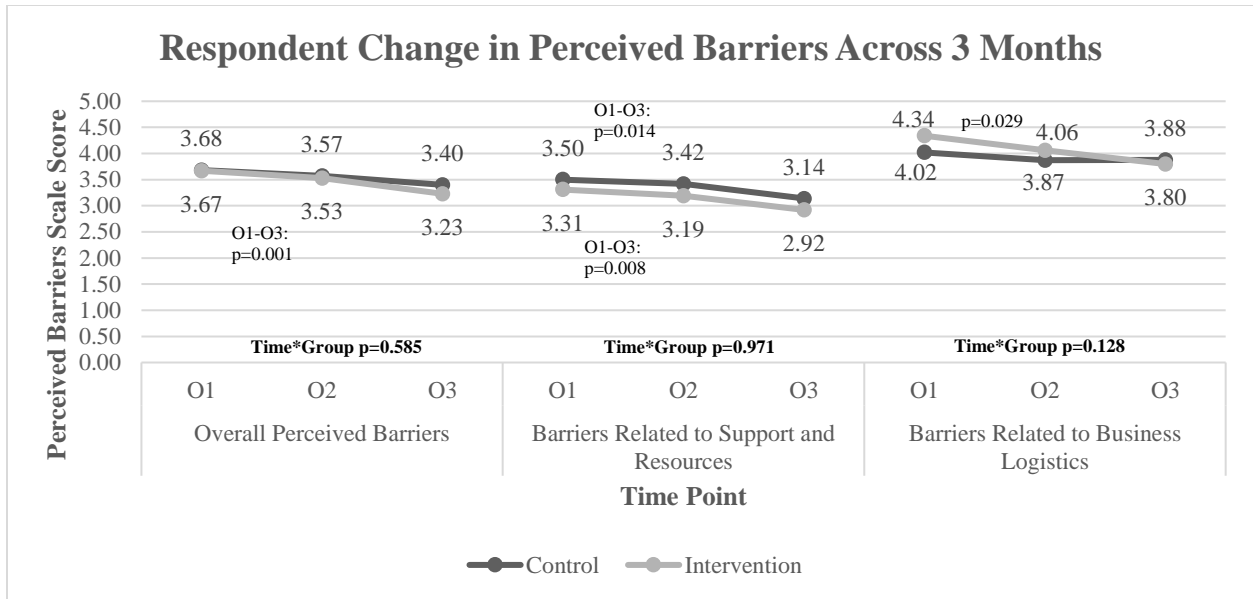[a] Based on results of mixed ANOVA with Bonferroni post-hoc tests.

Figure 4.9 Change in Mean Perceived Barriers Scale Scores Over 3-Month Study Period. Only statistically significant p-values within groups are shown.

Change in Behaviors

Hypotheses H6-7a stated that number of naloxone service structure activities completed and number of process activities engaged in by the end of the 3-month study period, respectively, will be greater among intervention compared to control group pharmacists. Furthermore, hypothesis H8a stated that change in number of naloxone prescriptions dispensed from baseline to 3-months will be greater among intervention compared to control group pharmacists. To assess this, behaviors were measured at O1 and O3 and included pharmacy-based naloxone service structure activity completion, naloxone service process activity engagement, and number of naloxone prescriptions dispensed. Each construct is presented separately below.

Structures

Respondent progress towards completing pharmacy-based naloxone service structure activities at each time point are described below in terms of frequency of completion level for each activity (Table 4.32).

219

Table 4.32 Progress Towards Completing Naloxone Service Structure Activities at O1 and O3

Question [a] *"In the past 3 months, I or my pharmacy staff…"*	n (%) [b]			
	O1 (N=64)		O3 (N=60)	
	C (N=32)	I (N=32)	C (N=30)	I (N=30)
Prepared an action plan for offering naloxone services				
No progress or not started	**13 (41.9)**	**11 (35.5)**	**7 (23.3)**	4 (13.3)
Minimal progress	7 (22.6)	5 (16.1)	3 (10.0)	**7 (23.3)**
Some progress	4 (12.9)	4 (12.9)	4 (13.3)	6 (20.0)
A fair amount of progress	2 (6.5)	2 (6.5)	5 (16.7)	4 (13.3)
A lot of progress	0	2 (6.5)	3 (10.0)	4 (13.3)
Almost completed	0	1 (3.2)	1 (3.3)	0
Completed	5 (16.1)	6 (19.4)	**7 (23.3)**	5 (16.7)
Established staff member roles for naloxone services				
No progress or not started	**17 (54.8)**	**14 (45.2)**	**9 (30.0)**	6 (20.0)
Minimal progress	7 (22.6)	3 (9.7)	5 (16.7)	5 (16.7)
Some progress	1 (3.2)	5 (16.1)	4 (13.3)	**7 (23.3)**
A fair amount of progress	0	2 (6.5)	1 (3.3)	3 (10.0)
A lot of progress	1 (3.2)	1 (3.2)	2 (6.7)	3 (10.0)
Almost completed	0	0	1 (3.3)	1 (3.3)
Completed	5 (16.1)	6 (19.4)	8 (26.7)	5 (16.7)
Selected a person who is in charge of naloxone services				
No progress or not started	**20 (64.5)**	**18 (58.1)**	**11 (36.7)**	**8 (26.7)**
Minimal progress	5 (16.1)	1 (3.2)	5 (16.7)	6 (20.0)
Some progress	2 (6.5)	4 (12.9)	3 (10.0)	5 (16.7)
A fair amount of progress	0	1 (3.2)	5 (16.7)	3 (10.0)
A lot of progress	0	1 (3.2)	1 (3.3)	2 (6.7)
Almost completed	0	1 (3.2)	0	1 (3.3)
Completed	4 (12.9)	5 (16.1)	5 (16.7)	5 (16.7)
Approached management, corporate, or owners to gain support				
No progress or not started	**14 (45.2)**	**12 (38.7)**	**10 (33.3)**	5 (16.7)
Minimal progress	5 (16.1)	5 (16.1)	3 (10.0)	1 (3.3)
Some progress	2 (6.5)	6 (19.4)	3 (1.0)	7 (23.3)
A fair amount of progress	1 (3.2)	2 (6.5)	3 (10.0)	4 (13.3)
A lot of progress	1 (3.2)	0	0	2 (6.7)
Almost completed	2 (6.5)	0	1 (3.3)	0

Completed	6 (19.4)	6 (19.4)	**10 (33.3)**	**11 (36.7)**
Prepared an outreach/marketing plan for naloxone				
No progress or not started	**20 (64.5)**	**20 (64.5)**	**15 (50.0)**	**14 (46.7)**
Minimal progress	4 (12.9)	5 (16.1)	2 (6.7)	12 (40.0)
Some progress	0	4 (12.9)	5 (16.7)	1 (3.3)
A fair amount of progress	2 (6.5)	0	1 (3.3)	3 (10.0)
A lot of progress	0	0	2 (6.7)	0
Almost completed	0	0	2 (6.7)	0
Completed	5 (16.1)	2 (6.5)	3 (10.0)	0
Decided which naloxone products to stock				
No progress or not started	**9 (29.0)**	5 (16.1)	8 (26.7)	2 (6.7)
Minimal progress	5 (16.1)	**8 (25.8)**	3 (10.0)	2 (6.7)
Some progress	3 (9.7)	5 (16.1)	3 (10.0)	5 (16.7)
A fair amount of progress	1 (3.2)	1 (3.2)	2 (6.7)	3 (10.0)
A lot of progress	0	3 (9.7)	1 (3.3)	3 (10.0)
Almost completed	0	0	1 (3.3)	2 (6.7)
Completed	13 (41.9)	9 (29.0)	**12 (40.0)**	**13 (43.3)**
Established naloxone stocking procedures				
No progress or not started	11 (35.5)	**8 (25.8)**	8 (26.7)	2 (6.7)
Minimal progress	2 (6.5)	7 (22.6)	5 (16.7)	2 (6.7)
Some progress	4 (12.9)	4 (12.9)	1 (3.3)	7 (23.3)
A fair amount of progress	2 (6.5)	1 (3.2)	2 (6.7)	4 (13.3)
A lot of progress	0	2 (6.5)	2 (6.7)	2 (6.7)
Almost completed	0	1 (3.2)	1 (3.3)	2 (6.7)
Completed	**12 (38.7)**	**8 (25.8)**	**11 (36.7)**	**11 (36.7)**
Set a goal or objective for naloxone services				
No progress or not started	**20 (64.5)**	**17 (54.8)**	**12 (40.0)**	6 (20.0)
Minimal progress	3 (9.7)	5 (16.1)	3 (10.0)	**9 (30.0)**
Some progress	1 (3.2)	1 (3.2)	3 (10.0)	7 (23.3)
A fair amount of progress	1 (3.2)	1 (3.2)	2 (6.7)	3 (10.0)
A lot of progress	0	2 (6.5)	0	1 (3.3)
Almost completed	0	0	4 (13.3)	0
Completed	6 (19.4)	5 (16.1)	6 (20.0)	4 (13.3)
Adjusted prescription dispensing workflow to allow for greater naloxone services activity				
No progress or not started	**21 (67.7)**	**23 (74.2)**	**15 (50.0)**	**14 (46.7)**

Minimal progress	5 (16.1)	4 (12.9)	4 (13.3)	8 (26.7)
Some progress	1 (3.2)	1 (3.2)	1 (3.3)	3 (10.0)
A fair amount of progress	1 (3.2)	1 (3.2)	3 (10.0)	2 (6.7)
A lot of progress	0	0	0	1 (3.3)
Almost completed	0	0	1 (3.3)	0
Completed	3 (9.7)	2 (6.5)	6 (20.0)	2 (6.7)
Arranged staff schedules to accommodate naloxone services				
No progress or not started	**24 (77.4)**	**26 (83.9)**	**17 (56.7)**	**19 (63.3)**
Minimal progress	4 (12.9)	3 (9.7)	4 (13.3)	7 (23.3)
Some progress	0	0	3 (10.0)	1 (3.3)
A fair amount of progress	0	1 (3.2)	0	1 (3.3)
A lot of progress	0	0	0	0
Almost completed	0	0	0	0
Completed	3 (9.7)	1 (3.2)	6 (20.0)	2 (6.7)
Established a procedure to identify patients who would benefit from naloxone				
No progress or not started	**19 (61.3)**	**17 (54.8)**	**9 (30.0)**	**8 (26.7)**
Minimal progress	6 (19.4)	3 (9.7)	5 (16.7)	7 (23.3)
Some progress	1 (3.2)	2 (6.5)	3 (10.0)	5 (16.7)
A fair amount of progress	0	0	2 (6.7)	3 (10.0)
A lot of progress	1 (3.2)	3 (9.7)	2 (6.7)	2 (6.7)
Almost completed	0	0	0	0
Completed	4 (12.9)	6 (19.4)	**9 (30.0)**	5 (16.7)
Established a procedure to document naloxone dispensing				
No progress or not started	**18 (58.1)**	**14 (45.2)**	**12 (40.0)**	**8 (26.7)**
Minimal progress	2 (6.5)	4 (12.9)	4 (13.3)	6 (20.0)
Some progress	2 (6.5)	2 (6.5)	1 (3.3)	3 (10.0)
A fair amount of progress	0	0	4 (13.3)	1 (3.3)
A lot of progress	0	2 (6.5)	0	3 (10.0)
Almost completed	0	1 (3.2)	0	1 (3.3)
Completed	9 (29.0)	8 (25.8)	9 (30.0)	**8 (26.7)**
Established a procedure to follow-up with patients if naloxone was not in stock				
No progress or not started	**20 (64.5)**	**18 (58.1)**	9 (30.0)	**10 (33.3)**
Minimal progress	1 (3.2)	3 (9.7)	5 (16.7)	4 (13.3)
Some progress	0	1 (3.2)	3 (10.0)	4 (13.3)

A fair amount of progress	2 (6.5)	1 (3.2)	1 (3.3)	4 (13.3)
A lot of progress	0	1 (3.2)	0	1 (3.3)
Almost completed	1 (3.2)	1 (3.2)	0	2 (6.7)
Completed	7 (22.6)	6 (19.4)	**12 (40.0)**	5 (16.7)
Developed the budget for naloxone services				
No progress or not started	**23 (74.2)**	**23 (74.2)**	**13 (43.3)**	**17 (56.7)**
Minimal progress	1 (3.2)	3 (9.7)	5 (16.7)	8 (26.7)
Some progress	0	0	2 (6.7)	1 (3.3)
A fair amount of progress	0	0	1 (3.3)	2 (6.7)
A lot of progress	2 (6.5)	0	0	0
Almost completed	0	1 (3.2)	0	2 (6.7)
Completed	5 (16.1)	4 (12.9)	9 (30.0)	0
Established a plan to continuously evaluate and improve the pharmacy's naloxone services				
No progress or not started	**22 (71.0)**	**23 (74.2)**	**12 (40.0)**	11 (36.7)
Minimal progress	3 (9.7)	3 (9.7)	6 (20.0)	**13 (43.3)**
Some progress	2 (6.5)	0	2 (6.7)	3 (10.0)
A fair amount of progress	0	1 (3.2)	2 (6.7)	2 (6.7)
A lot of progress	0	0	0	0
Almost completed	0	0	0	0
Completed	4 (12.9)	4 (12.9)	8 (26.7)	1 (3.3)
Established access to my state's Prescription Drug Monitoring Program (PDMP)				
No progress or not started	3 (9.7)	3 (9.7)	4 (13.3)	3 (10.0)
Minimal progress	0	0	1 (3.3)	1 (3.3)
Some progress	0	3 (9.7)	0	1 (3.3)
A fair amount of progress	0	1 (3.2)	1 (3.3)	1 (3.3)
A lot of progress	0	0	0	1 (3.3)
Almost completed	0	2 (6.5)	1 (3.3)	0
Completed	**28 (90.3)**	**22 (71.0)**	**23 (76.7)**	**23 (76.7)**

C=Control group, I=Intervention group

[a] On a Likert-type scale of 1 to 7, where 1=no progress and 7=completed.

[b] Percentages may differ due to item non-response.

Higher mean values represent more progress towards completing all activities, whereas lower mean values represent less progress. Among the 57 individuals who responded to both surveys, the mean structure activity completion index score ranged between 2.00 and 4.00 for both groups at each time point (Tables 4.33a-b). Specifically, the mean (SD) structure activity completion index score among the intervention group was 2.66 (1.49) at O1 and 3.39 (1.22) at O3. Among the control group, mean (SD) structure activity completion index scores were 2.73 (1.68) at O1 and 3.48 (2.09) at O3.

Changes in mean structure activity completion index scores across O1 and O3 were also assessed for the 57 individuals who responded to both surveys (Tables 4.33a-b, Figure 4.10). Values are mean (SD) unless stated otherwise. There was a statistically significant increase in overall structure activity completion index score within the intervention group from O1 to O3 (2.66 to 3.39, p=0.004). However, this change was not statistically significant compared to control (p=0.972). Therefore, when compared to control, the training program did not affect pharmacists' progress towards completion of pharmacy-based naloxone service structure activities over 3 months.

Table 4.33a Overall Effect of the Intervention on Progress Towards Structure Activity Completion

Structure Activity Completion		
Factor	F	p-value [a]
Time	18.554	<0.0005*
Time * Group	0.001	0.972
Group	0.038	0.846

Table 4.33b Change in Mean Structure Activity Completion Index Score in Control and Intervention Groups Over 3 Months (N=57)

	Overall Progress Towards Structure Activity Completion				
	Mean Activity Completion Index Scores at O1 and O3				
	Control (N=29)		Intervention (N=28)		
Time	Mean (SD)		Mean (SD)		
O1	2.73 (1.68)		2.66 (1.49)		
O3	3.48 (2.09)		3.39 (1.22)		
	Change in Activity Completion Within Groups				Between Groups
	Control (N=29)		Intervention (N=28)		
Time	Mean Difference (SE)	p-value [a]	Mean Difference (SE)	p-value [a]	p-value [a]
O1-O3	0.74 (0.24)	0.003*	0.73 (0.24)	0.004*	0.972

Significance at the 0.05 level indicated by *.
[a] Based on results of mixed ANOVA with Bonferroni post-hoc tests.
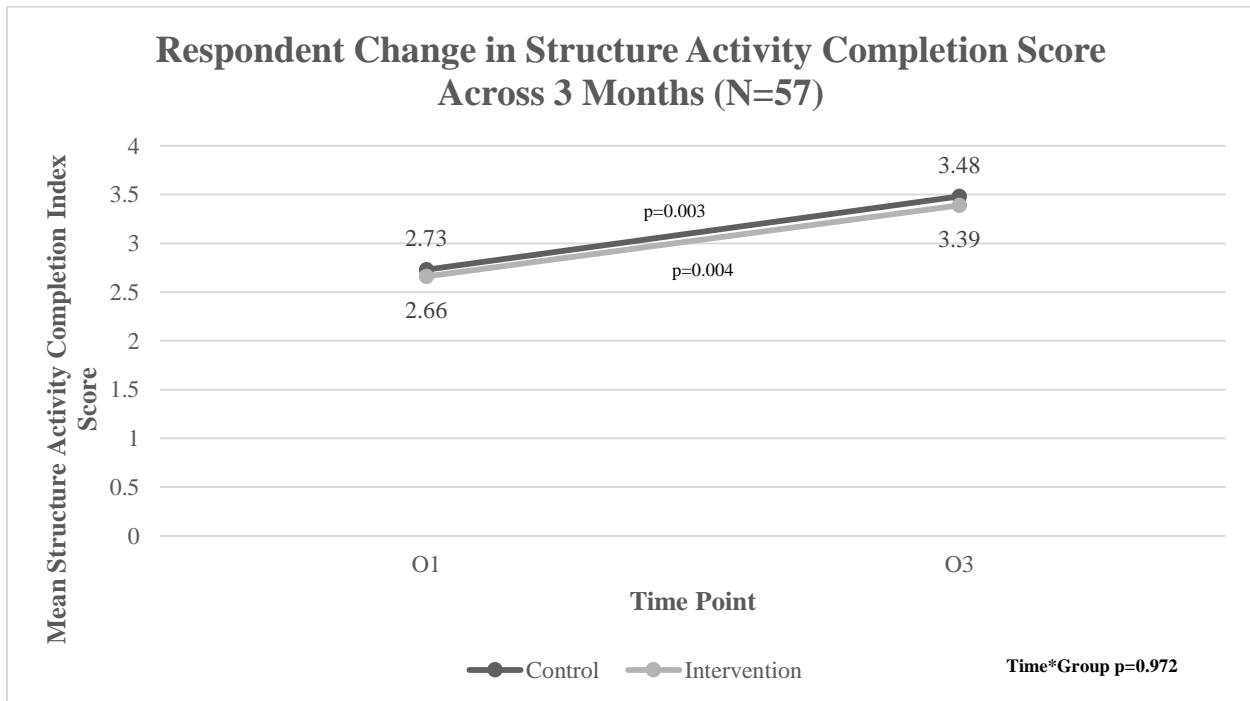
Figure 4.10 Change in Mean Structure Activity Completion Index Score Over 3-Month Study Period

Another way to look at implementation of naloxone service structure activities is to assess the number of activities that were completed versus never completed in control and intervention group pharmacies. The overall level of naloxone service structure implementation by the end of the 3-month study period in control and intervention group pharmacies is presented below (Table 4.34) based on number of structure activities completed.

No statistically significant differences between intervention and control pharmacies were found regarding frequency of task completion (Table 4.34). Of the 16 structure-based activities assessed, intervention pharmacies completed 3 activities and control pharmacies completed 4 activities on average ($p=0.737$) by the end of the 3-month intervention period. Furthermore, 7 intervention pharmacies and 9 control pharmacies completed at least half of the structure activities ($p=0.466$). The most frequently completed task was establishing access to Alabama's Prescription Drug Monitoring Program (PDMP), with 23 and 27 of intervention and control pharmacies, respectively, reporting it as "completed" ($p=0.253$). The least frequently completed task was preparing an outreach/marketing plan for naloxone services, with 26 and 23 of intervention and control pharmacies, respectively, reporting it as "never completed" ($p=0.253$).

In summary, hypothesis 6a stated that number of naloxone service structure activities completed by the end of the 3-month study period will be greater among intervention compared to control group pharmacists. We failed to reject the null hypothesis, and concluded that the training program had no effect on number of structure activities completed.

Table 4.34 Level of Naloxone Service Structure Implementation by the End of the 3-Month Study Period (N=57)

Structure Activities	Mean (SD) Median (IQR)		p-value [a]
	Control (N=29)	Intervention (N=28)	
Number Activities Completed **(16 Total Activities)**	5.90 (6.18) 4.00 (1.00-13.50)	4.68 (4.68) 3.00 (1.00-8.50)	0.737
	No. of Pharmacies, n (%)		p-value [d]
Level of Implementation			
Full 100% (16 activities completed)	4 (13.8)	1 (3.6)	0.466
Partial ≥50% (8-15 activities)	5 (17.2)	6 (21.4)	
Partial < 50% (0-7 activities)	20 (69.0)	21 (75.0)	
Structure Indicator	No. of Pharmacies, n (%) [b]		p-value [d]
	Control (n=29)	Intervention (n=28)	
Prepared an action plan for offering naloxone services			
Never completed [c]	20 (69.0)	20 (71.4)	1.000
Completed	9 (31.0)	8 (28.6)	
Established staff member roles for naloxone services			
Never completed	20 (69.0)	21 (75.0)	0.770
Completed	9 (31.0)	7 (25.0)	
Selected a person who is in charge of naloxone services			
Never completed	22 (75.9)	21 (75.0)	1.000
Completed	7 (24.1)	7 (25.0)	
Approached management, corporate, or owners to gain support			
Never completed	19 (65.5)	18 (64.3)	1.000
Completed	10 (34.5)	10 (35.7)	
Prepared an outreach/marketing plan for naloxone			
Never completed	23 (79.3)	26 (92.9)	0.253
Completed	6 (20.7)	2 (7.1)	
Decided which naloxone products to stock			
Never completed	14 (48.3)	13 (46.4)	1.000
Completed	15 (51.7)	15 (53.6)	
Established naloxone stocking procedures			
Never completed	16 (55.2)	15 (53.6)	1.000
Completed	13 (44.8)	13 (46.4)	

227

Set a goal or objective for naloxone services			
Never completed	21 (72.4)	22 (78.6)	0.760
Completed	8 (27.6)	6 (21.4)	
Adjusted prescription dispensing workflow to allow for greater naloxone services activity			0.179
Never completed	21 (72.4)	25 (89.3)	
Completed	8 (27.6)	3 (10.7)	
Arranged staff schedules to accommodate naloxone services			
Never completed	22 (75.9)	25 (89.3)	0.297
Completed	7 (24.1)	3 (10.7)	
Established a procedure to identify patients who would benefit from naloxone			0.565
Never completed	19 (65.5)	21 (75.0)	
Completed	10 (34.5)	7 (25.0)	
Established a procedure to document naloxone dispensing			
Never completed	16 (55.2)	18 (64.3)	0.592
Completed	13 (44.8)	10 (35.7)	
Established a procedure to follow-up with patients if naloxone was not in stock			0.585
Never completed	17 (58.6)	19 (67.9)	
Completed	12 (41.4)	9 (32.1)	
Developed the budget for naloxone services			
Never completed	20 (69.0)	24 (85.7)	0.207
Completed	9 (31.0)	4 (14.3)	
Established a plan to continuously evaluate and improve the pharmacy's naloxone services			0.331
Never completed	21 (72.4)	24 (85.7)	
Completed	8 (27.6)	4 (14.3)	
Established access to my state's Prescription Drug Monitoring Program (PDMP)			0.253
Never completed	2 (6.9)	5 (17.9)	
Completed	27 (93.1)	23 (82.1)	

[a] Based on two-sided Mann-Whitney U test with a priori alpha level of 0.05.

[b] Number of pharmacies that completed structure activities during the 3-month study period. Percentages may differ due to item non-response.

[c] Never completed = no activity or in progress.

[d] Based on a Fisher's exact test with a priori alpha level of 0.05.

Processes

Respondent engagement in pharmacy-based naloxone service process activities at each time point are described below in terms of frequency of engagement level for each activity (Table 4.35).

Table 4.35 Frequency of Engagement in Naloxone Service Process Activities at O1 and O3

Question [a] *"In the past 3 months, I or my pharmacy staff…"*	n (%) [b]			
	O1 (N=64)		O3 (N=60)	
	C (N=32)	I (N=32)	C (N=30)	I (N=30)
Conducted staff meetings to discuss plans for naloxone services				
Never	**23 (74.2)**	**18 (58.1)**	**11 (36.7)**	**13 (43.3)**
Very infrequently	3 (9.7)	9 (29.0)	**11 (36.7)**	5 (16.7)
Infrequently	3 (9.7)	1 (3.2)	4 (13.3)	3 (10.0)
Sometimes	2 (6.5)	3 (9.7)	3 (10.0)	5 (16.7)
Fairly Often	0	0	1 (3.3)	4 (13.3)
Frequently	0	0	0	0
Very frequently	0	0	0	0
Identified patients who could benefit from naloxone based on medication profile				
Never	**13 (41.9)**	**12 (38.7)**	5 (16.7)	6 (20.0)
Very infrequently	5 (16.1)	6 (19.4)	**6 (20.0)**	2 (6.7)
Infrequently	2 (6.5)	1 (3.2)	5 (16.7)	1 (3.3)
Sometimes	4 (12.9)	6 (19.4)	**6 (20.0)**	**12 (40.0)**
Fairly Often	3 (9.7)	1 (3.2)	1 (3.3)	3 (10.0)
Frequently	1 (3.2)	2 (6.5)	5 (16.7)	3 (10.0)
Very frequently	3 (9.7)	3 (9.7)	2 (6.7)	3 (10.0)
Identified patients who could benefit from naloxone based on medical history screening				
Never	**17 (54.8)**	**14 (45.2)**	**8 (26.7)**	**8 (26.7)**
Very infrequently	2 (6.5)	5 (16.1)	7 (23.3)	2 (6.7)
Infrequently	3 (9.7)	0	2 (6.7)	5 (16.7)
Sometimes	5 (16.1)	6 (19.4)	5 (16.7)	**8 (26.7)**
Fairly Often	2 (6.5)	1 (3.2)	2 (6.7)	3 (10.0)
Frequently	1 (3.2)	2 (6.5)	5 (15.2)	2 (6.7)
Very frequently	1 (3.2)	3 (9.7)	1 (3.0)	2 (6.7)
Identified patients who could benefit from naloxone based on non-prescription consultations				
Never	**23 (74.2)**	**20 (64.5)**	**13 (43.3)**	**13 (43.3)**
Very infrequently	6 (19.4)	6 (19.4)	6 (20.0)	5 (16.7)
Infrequently	1 (3.2)	2 (6.5)	2 (6.7)	7 (23.3)
Sometimes	0	2 (6.5)	5 (16.7)	4 (13.3)
Fairly Often	1 (3.0)	0	1 (3.3)	1 (3.3)

230

Frequently	0	0	3 (10.0)	0
Very frequently	0	1 (3.2)	0	0
Stocked / continued stocking at least one naloxone dosage form				
Never	8 (25.8)	6 (19.4)	3 (10.0)	2 (6.7)
Very infrequently	3 (9.7)	1 (3.2)	2 (6.7)	2 (6.7)
Infrequently	0	0	2 (6.7)	2 (6.7)
Sometimes	0	2 (6.5)	1 (3.3)	1 (3.3)
Fairly Often	1 (3.2)	4 (12.9)	3 (10.0)	3 (10.0)
Frequently	3 (9.7)	5 (16.1)	7 (23.3)	1 (3.3)
Very frequently	**16 (51.6)**	**13 (41.9)**	**12 (40.0)**	**19 (63.3)**
Educated patient(s) or caregiver(s) on how to recognize an opioid overdose				
Never	**9 (29.0)**	**10 (32.3)**	4 (13.3)	3 (10.0)
Very infrequently	6 (19.4)	3 (9.7)	3 (10.0)	4 (13.3)
Infrequently	4 (12.9)	5 (16.1)	4 (13.3)	2 (6.7)
Sometimes	**9 (29.0)**	6 (19.4)	**12 (40.0)**	**7 (23.3)**
Fairly Often	1 (3.2)	3 (9.7)	1 (3.3)	**7 (23.3)**
Frequently	1 (3.2)	3 (9.7)	4 (13.3)	2 (6.7)
Very frequently	1 (3.2)	1 (3.2)	2 (6.7)	5 (16.7)
Counseled patient(s) or caregiver(s) on how to correctly administer naloxone				
Never	**9 (29.0)**	7 (22.6)	8 (26.7)	6 (20.0)
Very infrequently	6 (19.4)	**8 (25.8)**	3 (10.0)	2 (6.7)
Infrequently	2 (6.5)	4 (12.9)	4 (13.3)	3 (10.0)
Sometimes	**9 (29.0)**	6 (19.4)	**9 (30.0)**	**8 (26.7)**
Fairly Often	2 (6.5)	2 (6.5)	2 (6.7)	4 (13.3)
Frequently	2 (6.5)	4 (12.9)	3 (10.0)	5 (16.7)
Very frequently	1 (3.2)	0	1 (3.3)	2 (6.7)
Provided naloxone via a physician's prescription for a patient taking high-dose prescription opioids				
Never	**10 (32.3)**	**7 (22.6)**	4 (13.3)	6 (20.0)
Very infrequently	4 (12.9)	**7 (22.6)**	5 (16.7)	4 (13.3)
Infrequently	3 (9.7)	5 (16.1)	**9 (30.0)**	3 (10.0)
Sometimes	7 (22.6)	4 (12.9)	6 (20.0)	**7 (23.3)**
Fairly Often	5 (16.1)	5 (16.1)	2 (6.7)	6 (20.0)
Frequently	2 (6.5)	1 (3.2)	4 (13.3)	1 (3.3)
Very frequently	0	2 (6.5)	0	3 (10.0)

Provided naloxone via a physician's prescription for a patient with a history of illicit opioid use				
Never	**18 (58.1)**	**20 (64.5)**	**11 (36.7)**	**17 (56.7)**
Very infrequently	5 (16.1)	7 (22.6)	5 (16.7)	5 (16.7)
Infrequently	3 (9.7)	3 (9.7)	7 (23.3)	3 (10.0)
Sometimes	3 (9.7)	1 (3.2)	5 (16.7)	5 (16.7)
Fairly Often	1 (3.2)	0	0	0
Frequently	1 (3.2)	0	2 (6.7)	0
Very frequently	0	0	0	0
Provided naloxone via Alabama's statewide standing order for a patient taking high-dose prescription opioids				
Never	**21 (67.7)**	**18 (58.1)**	**16 (53.3)**	**11 (36.7)**
Very infrequently	3 (9.7)	3 (9.7)	2 (6.7)	5 (16.7)
Infrequently	2 (6.5)	4 (12.9)	4 (13.3)	5 (16.7)
Sometimes	4 (12.9)	2 (6.5)	3 (10.0)	5 (16.7)
Fairly Often	0	1 (3.2)	1 (3.3)	1 (3.3)
Frequently	0	3 (9.7)	3 (10.0)	1 (3.3)
Very frequently	1 (3.2)	0	1 (3.3)	2 (6.7)
Provided naloxone via Alabama's statewide standing order for a patient with a history of illicit opioid use				
Never	**25 (80.6)**	**25 (80.6)**	**19 (63.3)**	**17 (56.7)**
Very infrequently	2 (6.5)	3 (9.7)	2 (6.7)	6 (20.0)
Infrequently	2 (6.5)	3 (9.7)	7 (23.3)	5 (16.7)
Sometimes	2 (6.5)	0	1 (3.3)	2 (6.7)
Fairly Often	0	0	1 (3.3)	0
Frequently	0	0	0	0
Very frequently	0	0	0	0
Initiated a conversation with a patient or caregiver about the benefits of naloxone				
Never	**10 (32.3)**	6 (19.4)	6 (20.0)	4 (13.3)
Very infrequently	6 (19.4)	**10 (32.3)**	5 (16.7)	3 (10.0)
Infrequently	2 (6.5)	2 (6.5)	3 (10.0)	5 (16.7)
Sometimes	9 (29.0)	5 (16.1)	**10 (33.3)**	**6 (20.0)**
Fairly Often	1 (3.2)	2 (6.5)	2 (6.7)	**4 (20.0)**
Frequently	3 (9.7)	4 (12.9)	3 (10.0)	5 (16.7)
Very frequently	0	2 (6.5)	1 (3.3)	3 (10.0)
Billed a third-party payer for the dispensing of naloxone				

232

Never	**9 (29.0)**	**10 (32.3)**	5 (16.7)	**5 (16.7)**
Very infrequently	3 (9.7)	8 (25.8)	2 (6.7)	4 (13.3)
Infrequently	5 (16.1)	1 (3.2)	3 (10.0)	4 (13.3)
Sometimes	5 (16.1)	2 (6.5)	**13 (43.3)**	5 (16.7)
Fairly Often	5 (16.1)	5 (16.1)	1 (3.3)	2 (6.7)
Frequently	2 (6.5)	2 (6.5)	6 (20.0)	**5 (16.7)**
Very frequently	2 (6.5)	3 (9.7)	0	**5 (16.7)**
Notified an individual's physician after naloxone was dispensed				
Never	**26 (83.9)**	**17 (54.8)**	**18 (60.0)**	**14 (46.7)**
Very infrequently	2 (6.5)	6 (19.4)	4 (13.3)	9 (30.0)
Infrequently	1 (3.2)	2 (6.5)	1 (3.3)	5 (16.7)
Sometimes	0	4 (12.9)	5 (16.7)	0
Fairly Often	1 (3.2)	0	1 (3.3)	1 (3.3)
Frequently	0	1 (3.2)	1 (3.3)	1 (3.3)
Very frequently	1 (3.2)	1 (3.2)	0	0
Marketed the pharmacy's naloxone services using in-store advertisements like posters, flyers, or bag stuffers				
Never	**24 (77.4)**	**26 (83.9)**	**24 (80.0)**	**23 (76.7)**
Very infrequently	2 (6.5)	3 (9.7)	1 (3.3)	3 (10.0)
Infrequently	2 (6.5)	1 (3.2)	0	1 (3.3)
Sometimes	0	0	0	2 (6.7)
Fairly Often	1 (3.2)	0	3 (10.0)	0
Frequently	0	1 (3.2)	1 (3.3)	1 (3.3)
Very frequently	2 (6.5)	0	1 (3.3)	0
Marketed the pharmacy's naloxone services using external media like radio, newspaper, or TV advertisements				
Never	**28 (90.3)**	**28 (90.3)**	**25 (83.3)**	**25 (83.3)**
Very infrequently	0	2 (6.5)	1 (3.3)	3 (10.0)
Infrequently	1 (3.2)	0	1 (3.3)	1 (3.3)
Sometimes	1 (3.2)	1 (3.2)	2 (6.7)	1 (3.3)
Fairly Often	1 (3.2)	0	1 (3.3)	0
Frequently	0	0	0	0
Very frequently	0	0	0	0

C=Control group, I=Intervention group

[a] On a Likert-type scale of 1 to 7, where 1=never and 7=very frequently.

[b] Percentages may differ due to item non-response.

233

Higher mean values represent more frequent engagement in all activities, whereas lower mean values represent less frequent engagement. Among the 57 individuals who responded to both surveys, the mean process activity engagement index score ranged between 2.00 and 3.00 for both groups at each time point (Tables 4.36a-b). Specifically, the mean (SD) process activity engagement index score among the intervention group was 2.35 (1.04) at O1 and 3.03 (0.94) at O3. Among the control group, mean (SD) process activity engagement index scores were 2.38 (1.06) at O1 and 2.74 (1.14) at O3.

Changes in mean process activity engagement index scores across O1 and O3 were also assessed for the 57 individuals who responded to both surveys (Tables 4.36a-b, Figure 4.11). Values are mean (SD) unless stated otherwise. There was a statistically significant increase in overall process activity engagement index score within the intervention group from O1 to O3 (2.35 to 3.03, p<0.0005). However, this change was not statistically significant compared to control (p=0.151). Therefore, when compared to control, the training program did not affect pharmacists' frequency of engagement in pharmacy-based naloxone service process activities over 3 months.

Table 4.36a Overall Effect of the Intervention on Process Activity Engagement

Process Activity Engagement		
Factor	**F**	**p-value [a]**
Time	22.299	<0.0005
Time * Group	2.123	0.151
Group	0.230	0.633

Table 4.36b Change in Mean Process Activity Engagement Index Score in Control and Intervention Groups Over 3 Months (N=57)

	Overall Process Activity Engagement				
	Mean Activity Engagement Index Scores at O1 and O3				
	Control (N=29)		Intervention (N=28)		
Time	Mean (SD)		Mean (SD)		
O1	2.38 (1.06)		2.35 (1.04)		
O3	2.74 (1.14)		3.03 (0.94)		
	Change in Activity Engagement Within Groups				Between Groups
	Control (N=29)		Intervention (N=28)		
Time	Mean Difference (SE)	p-value [a]	Mean Difference (SE)	p-value [a]	p-value [a]
O1-O3	0.36 (0.15)	0.024*	0.68 (0.16)	<0.0005*	0.151

Significance at the 0.05 level indicated by *.
[a] Based on results of mixed ANOVA with Bonferroni post-hoc tests.
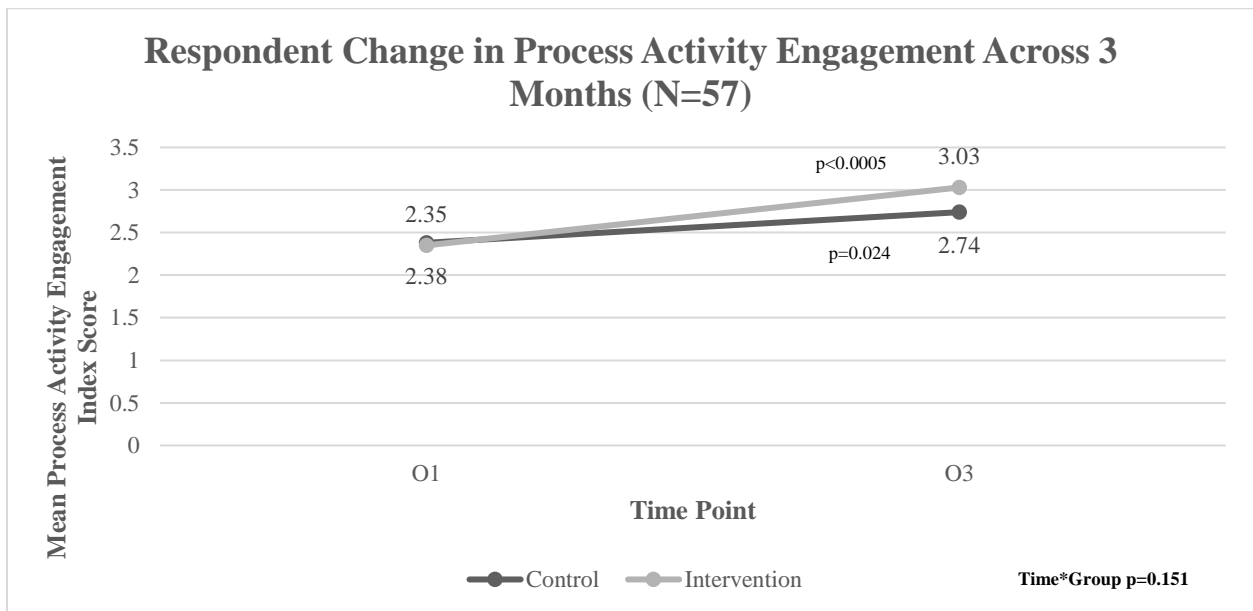
Figure 4.11 Change in Mean Process Activity Engagement Index Score Over 3-Month Study Period

Another way to look at implementation of naloxone service process activities is to assess the number of activities that were engaged versus never engaged in control and intervention group pharmacies. The overall level of naloxone service process implementation by the end of the 3-month study period in control and intervention group pharmacies is presented below (Table 4.37) based on number of process activities engaged.

No statistically significant differences between intervention and control pharmacies were found regarding frequency of activity engagement (Table 4.37). Of the 16 process-based activities assessed, intervention pharmacies engaged in 12 activities and control pharmacies engaged in 11 activities on average (p=0.670) by the end of the 3-month intervention period. Furthermore, 22 intervention pharmacies and 22 control pharmacies engaged in at least half of the structure activities (p=1.000). The 2 most frequently engaged tasks were: stocking at least one dosage form of naloxone, with 27 and 26 of intervention and control pharmacies, respectively, reporting it as "engaged" (p=0.611); and educating patients or caregivers on how to recognize an opioid overdose, with 26 and 27 of intervention and control pharmacies, respectively, reporting it as "engaged" (p=1.000). The least frequently engaged task was marketing the pharmacy's naloxone services using external media like radio, newspaper, or TV advertisements, with 23 and 25 of intervention and control pharmacies, respectively, reporting it as "never engaged" (p=0.730).

In summary, hypothesis 7a stated that number of naloxone process activities engaged in by the end of the 3-month study period will be greater among intervention compared to control group pharmacists. We failed to reject the null hypothesis, and concluded that the training program had no effect on number of process activities engaged.

Table 4.37 Level of Naloxone Service Process Implementation by the End of the 3-Month Study Period (N=57)

Process Activities	Mean (SD) Median (IQR)		p-value [a]
	Control (N=29)	Intervention (N=28)	
Number Activities Engaged **(16 Total Activities)**	10.69 (4.10) 11.00 (7.50-14.00)	11.14 (3.93) 12.00 (10.00-14.00)	0.670
	No. of Pharmacies, n (%)		p-value [d]
Level of Implementation Full 100% (16 activities engaged) Partial ≥50% (8-15 activities) Partial < 50% (0-7 activities)	3 (10.3) 19 (65.5) 7 (24.1)	3 (10.7) 19 (67.9) 6 (21.4)	1.000
Structure Indicator	No. of Pharmacies, n (%) [b]		p-value [d]
	Control (N=29)	Intervention (N=28)	
Conducted staff meetings to discuss plans for naloxone services Never engaged [c] Engaged	10 (34.5) 19 (65.5)	8 (28.6) 20 (71.4)	0.777
Identified patients who could benefit from naloxone based on medication profile Never engaged Engaged	4 (13.8) 25 (86.2)	5 (17.9) 23 (82.1)	0.730
Identified patients who could benefit from naloxone based on medical history screening Never engaged Engaged	7 (24.1) 22 (75.9)	6 (21.4) 22 (78.6)	1.000
Identified patients who could benefit from naloxone based on non-prescription consultations Never engaged Engaged	11 (37.9) 18 (62.1)	10 (35.7) 18 (64.3)	1.000
Stocked / continued stocking at least one naloxone dosage form Never engaged Engaged	3 (10.3) 26 (89.7)	1 (3.6) 27 (96.4)	0.611
Educated patient(s) or caregiver(s) on how to recognize an opioid overdose Never engaged Engaged	2 (6.9) 27 (93.1)	2 (7.1) 26 (92.9)	1.000
Counseled patient(s) or caregiver(s) on how to correctly administer naloxone Never engaged Engaged	4 (13.8) 25 (86.2)	2 (7.1) 26 (92.9)	0.670

Provided naloxone via a physician's prescription for a patient taking high-dose prescription opioids			0.470
Never engaged	3 (10.3)	5 (17.9)	
Engaged	26 (89.7)	23 (82.1)	
Provided naloxone via a physician's prescription for a patient with a history of illicit opioid use			0.175
Never engaged	8 (27.6)	13 (46.4)	
Engaged	21 (72.4)	15 (53.6)	
Provided naloxone via Alabama's statewide standing order for a patient taking high-dose prescription opioids			0.289
Never engaged	15 (51.7)	10 (35.7)	
Engaged	14 (48.3)	18 (64.3)	
Provided naloxone via Alabama's statewide standing order for a patient with a history of illicit opioid use			0.596
Never engaged	18 (62.1)	15 (53.6)	
Engaged	11 (37.9)	13 (46.4)	
Initiated a conversation with a patient or caregiver about the benefits of naloxone			0.423
Never engaged	5 (17.2)	2 (7.1)	
Engaged	24 (82.8)	26 (92.9)	
Billed a third-party payer for the dispensing of naloxone			1.000
Never engaged	4 (13.8)	3 (10.7)	
Engaged	25 (86.2)	25 (89.3)	
Notified an individual's physician after naloxone was dispensed			0.289
Never engaged	15 (51.7)	10 (35.7)	
Engaged	14 (48.3)	18 (64.3)	
Marketed the pharmacy's naloxone services using in-store advertisements like posters, flyers, or bag stuffers			0.770
Never engaged	20 (69.0)	21 (75.0)	
Engaged Never engaged	9 (31.0)	7 (25.0)	
Marketed the pharmacy's naloxone services using external media like radio, newspaper, or TV advertisements			0.730
Never engaged	25 (86.2)	23 (82.1)	
Engaged	4 (13.8)	5 (17.9)	

[a] Based on two-sided Mann-Whitney U test with a priori alpha level of 0.05.

[b] Number of pharmacies that engaged in process activities at any time during the 3-month study period. Percentages may differ due to item non-response.

[c] Engaged=engaged in process activities at any time over 3 months. Never Engaged=never engaged in process activities at any time over 3 months.

[d] Based on a Fisher's exact test with a priori alpha level of 0.05.

Number of Naloxone Prescriptions Dispensed

The number of pharmacies that stocked naloxone as well as the number of naloxone prescriptions dispensed was measured at O1 and O3. Frequencies of naloxone services offered and particular dosage forms stocked are reported descriptively at O1 and O3 (Table 4.38). The change in number of naloxone prescriptions dispensed in control and intervention groups over the 3-month study period was also assessed (Table 4.39).

The majority of respondents' pharmacies offered naloxone services at both O1 and O3 in control and intervention groups (Table 4.38). The most frequently stocked dosage form was the commercially available nasal spray (Narcan®), while the least frequently stocked dosage form was the pre-filled syringe (PFS). The majority of pharmacies in both groups stocked at least one form of naloxone at both O1 and O3.

Table 4.38 Frequency of Pharmacies Offering Naloxone Services and Stocking Naloxone Over 3-Month Study Period (N=57)

Question	n (%)			
	O1		O3	
	C (N=29)	I (N=28)	C (N=29)	I (N=28)
Do you currently offer naloxone services at your pharmacy?				
Yes	24 (82.8)	20 (71.4)	25 (86.2)	23 (82.1)
No	5 (17.2)	8 (28.6)	4 (13.8)	5 (17.9)
During the past 3 months, which naloxone dosage forms were stocked in your pharmacy?				
Nasal spray (Narcan®)	20 (71.4)	19 (70.4)	20 (69.0)	23 (82.1)
Auto-injector (Evzio®)	4 (14.3)	5 (18.5)	12 (41.4)	8 (28.6)
Vial for intramuscular (IM) injection + syringe	2 (7.1)	7 (25.9)	3 (10.3)	8 (28.6)
Pre-filled syringe (PFS) +/- MAD	2 (7.1)	5 (17.9)	5 (17.2)	2 (7.1)
No. Pharmacies that Stocked at Least One Dosage Form of Naloxone				
Yes	22 (75.9)	21 (75.0)	24 (82.8)	26 (92.9)
No	7 (24.1)	7 (25.0)	5 (17.2)	2 (7.1)

C=Control group, I=Intervention group, MAD=mucosal atomizer device

Regarding the change in number of naloxone prescriptions dispensed before and after the intervention (Table 4.39, Figure 4.12), this was assessed for each of 4 naloxone dosage forms as well as overall (total). In unadjusted analyses, there were no statistically significant changes in the number of Narcan®, Evzio®, naloxone vial, or naloxone pre-filled syringes dispensed within the intervention group from O1 to O3. There was a statistically significant increase in the total number of naloxone prescriptions dispensed in the intervention group from O1 to O3 (3.70 to 4.50, p=0.028). However, this change was not statistically significant compared to control (p=0.286).

Table 4.39 Number Naloxone Prescriptions Dispensed in Control and Intervention Groups Over 3 Months (N=57)

| Dosage Form | Naloxone Prescriptions Dispensed [c] Mean (SD) Median (IQR) | | | | | | Change in Naloxone Rx's O1-O3 Mean (SD) Median (IQR) | | |
| | Control (N=29) | | | Intervention (N=28) | | | | | |
	O1	O3	p-value [a]	O1	O3	p-value [a]	Control (N=29)	Intervention (N=28)	p-value [b]
Narcan®	1.57 (1.48) 1.00 (0-3.00)	1.72 (2.28) 1.00 (0-3.00)	0.891	2.41 (4.47) 1.00 (0-3.00)	3.61 (4.70) 2.00 (0-6.00)	0.091	0.18 (2.33) 0	1.15 (5.21) 0	0.201
Evzio®	0.18 (0.61) 0	0.24 (0.51) 0	0.531	0.70 (2.30) 0	0.54 (1.95) 0	1.000	0.07 (0.72) 0	-0.15 (1.54) 0	0.373
Vial + syringe	0.11 (0.42) 0	0.03 (0.19) 0	0.750	0.15 (0.53) 0	0.18 (0.55) 0	1.000	-0.07 (0.47) 0	-0.04 (0.71) 0	0.937
PFS +/- MAD	0.18 (0.95) 0	0.31 (0.19) 0	0.125	0.44 (1.81) 0	0.18 (0.95) 0	1.000	0.14 (0.36) 0	-0.26 (1.79) 0	0.210
Total	2.04 (1.79) 2.00 (0-3.00)	2.31 (2.98) 2.00 (0-3.00)	0.513	3.70 (7.65) 1.00 (0-5.00)	4.50 (6.11) 3.00 (0-7.00)	0.028*	0.32 (2.58) 0 (0-1.75)	0.70 (7.34) 0 (0-3.00)	0.286

[a] Based on a two-sided Wilcoxon Signed Rank test for paired data with a priori alpha level of 0.05. Significance denoted by *.

[b] Based on a two-sided Mann-Whitney U test with a priori alpha level of 0.05.

[c] Number of naloxone dosage forms stocked out of 4 possible dosage forms.
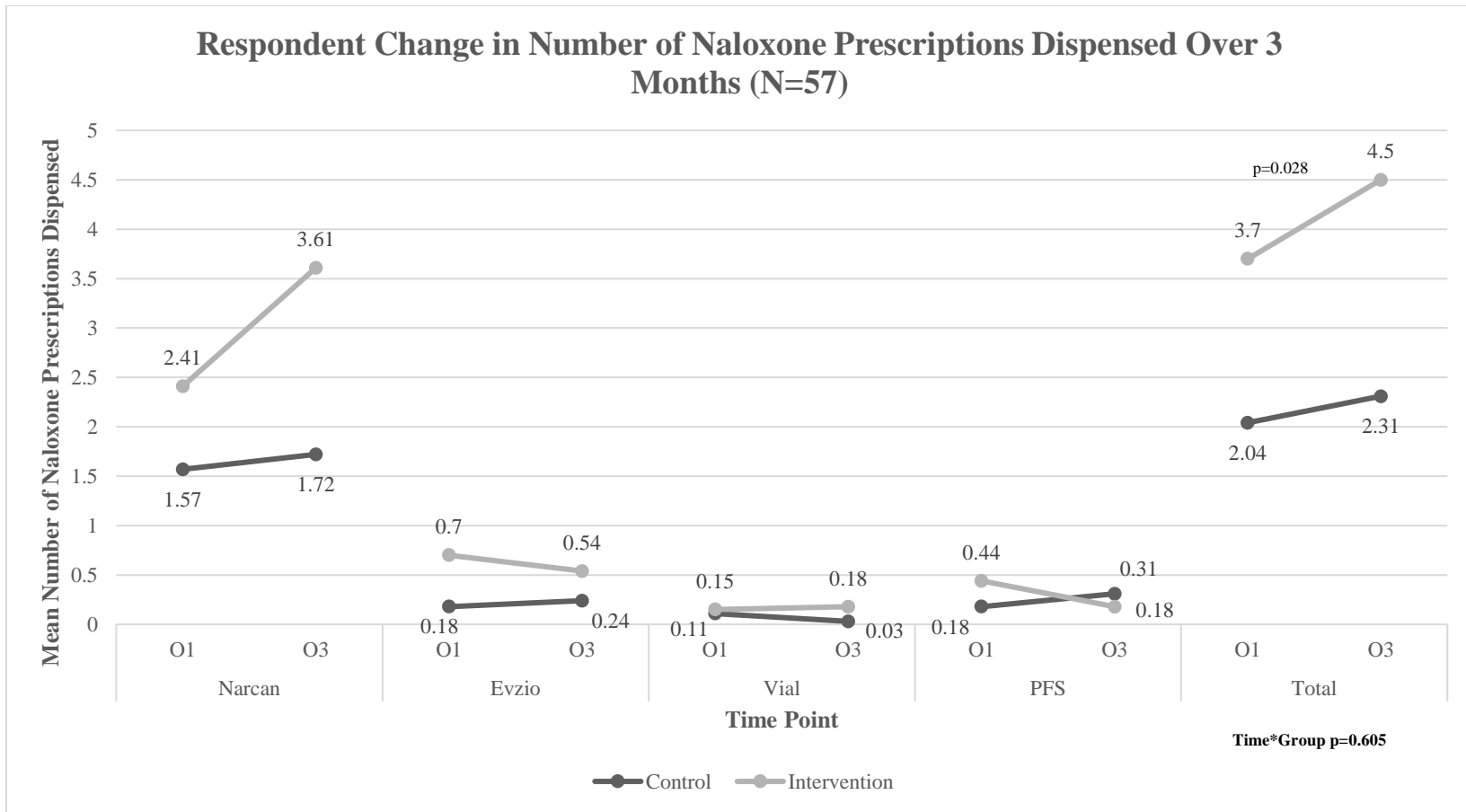
Figure 4.12 Change in Mean Number of Naloxone Prescriptions Dispensed Over 3-Month Study Period. Only statistically significant p-values within groups are shown.

In adjusted analyses, the training program had a positive effect on the total number of naloxone prescriptions dispensed among intervention versus control pharmacies (Table 4.40). Specifically, the change in total naloxone prescriptions dispensed from O1 to O3 was 1.33-fold higher among intervention compared to control pharmacies. However, this effect was not statistically significant (p=0.365). Participant and practice-level characteristics were controlled for, including: sex, race, and years practicing pharmacy (participant-level); and prescription volume, opioid-specific prescription volume, pharmacy type, and rurality (practice-level). Inclusion of the aforementioned covariates did not alter the conclusion regarding the effect of the intervention. Therefore, when compared to control, the training program did not affect number of naloxone prescriptions dispensed over 3 months.

In summary, hypothesis 8a stated that change in number of naloxone prescriptions dispensed from baseline to 3-months will be greater among intervention compared to control group pharmacists. We failed to reject the null hypothesis, and concluded that the training program had no effect on number of naloxone prescriptions dispensed.

Table 4.40. Relationship Between the EmpoweringCommunityPharmacists Program and Total Number of Naloxone Prescriptions Dispensed Over 3 Months (N=57)[a,b]

Parameter[c]	Exp(β)	Exp(95% CI)	p-value
Group (ref=control)	1.91	1.08, 3.36	0.025
Time (ref=O1)	1.13	0.73, 1.75	0.580
Group*Time	1.33	0.72, 2.48	0.365

$LogE(Number\ Naloxone\ Rx)_{i,j} = -0.94 + 0.65\ Group_{i,j} + 0.12\ Time_{i,j} + 0.29\ Group*Time_{i,j}$
$i=1,2...57; j=1,2$

$Time_{ij} \begin{cases} 0:O1 \\ 1:O3 \end{cases}$

$Group_{ij} \begin{cases} 0:control \\ 1:intervention \end{cases}$

[a]Results of generalized estimating equation (GEE) analyses utilizing a negative binomial distribution with log-link function. Dependent variable=number naloxone prescriptions. Independent variables=Group(intervention, control), Time(O1, O3), Group*Time.
[b]Controlling for covariates prescription volume, opioid-specific prescription volume, rurality, pharmacy type, sex, race and years in pharmacy practice did not significantly alter conclusions regarding the effect of the intervention.
[c]Reference level: Group=control, Time=O1.

4.2.4 Association of Knowledge, Intention, Beliefs and Behaviors

Regression analyses were conducted in order to assess the relationship between outcome measures reported in the preceding sections, according to a priori hypotheses presented in the Methods section. Multicollinearity between predictors was not detected (VIF < 10). Relationships reported below include:

1. The association of knowledge, intention, confidence, attitudes, and perceived barriers with the number of naloxone service structure activities completed from O1 to O3.

2. The association of knowledge, intention, confidence, attitudes, and perceived barriers with the number of naloxone service process activities engaged in from O1 to O3.

3. The association of knowledge, intention, confidence, attitudes, and perceived barriers with the number of naloxone prescriptions dispensed from O1 to O3.

4.2.4.1 Number of Structure Activities Completed

Hypothesis H9a stated that knowledge, intention, and beliefs (perceived barriers, attitudes, confidence) will be associated with number of naloxone service structure activities completed across 3 months. In regression analyses, two models were examined to assess potential differences in effect based on overall/aggregate scale predictors (Model 1) versus detailed scale predictors (Model 2). In Model 1, results showed that respondent confidence scores were positively associated and perceived barriers scores were negatively associated with the number of naloxone service structure activities completed among intervention and control pharmacies from O1 to O3 (Table 4.41). Specifically, the number of structure activities completed was 1.50 higher and 0.57 lower for every 1-point increase in confidence (p=0.016) and perceived barriers (p<0.0005) scores, respectively. Participant and practice-level characteristics were controlled for, including: sex, race, and years practicing pharmacy

244

(participant-level); and prescription volume, opioid-specific prescription volume, pharmacy type, and rurality (practice-level). Only statistically significant covariates were retained in the final model. Pharmacist knowledge about naloxone, intention to provide naloxone services, and attitudes regarding naloxone services were not associated with number of structure activities completed.

When examining detailed sub-scales in Model 2, we found that attitudes regarding prescription opioid misuse, barriers regarding support and resources, and barriers regarding business logistics were negatively associated with number of structure activities completed. Specifically, the number of structure activities completed was 0.67, 0.66, and 0.83 lower for every 1-point increase in attitudes about prescription opioid misuse (p=0.011), barriers regarding support and resources (p=0.005), and barriers regarding business logistics scores (p=0.046). Knowledge, intention, attitudes regarding illicit opioid misuse, confidence regarding patient-oriented activities, and confidence regarding business-oriented activities were not associated with number of structure activities completed.

In summary, hypothesis H9a stated that knowledge, intention, and beliefs (perceived barriers, attitudes, confidence) will be associated with number of naloxone service structure activities completed across 3 months. We failed to reject the null hypothesis, and concluded that knowledge, intention, confidence, attitudes, and perceived barriers are not all associated with number of structure activities completed.

Table 4.41 Relationship Between Knowledge, Intention, Confidence, and Perceived Barriers with Number of Structure Activities Completed Over 3 Months (N=57)

Model 1 [a,b]			
Parameter[c]	**Exp(β)**	**Exp(95% CI)**	**p-value**
Group (ref=control)	0.75	0.47, 1.19	0.226
Time (ref=O1)	1.35	1.02, 1.78	0.037*
Group*Time	0.92	0.64, 1.34	0.680
Knowledge	0.99	0.98, 1.00	0.109
Intention	1.00	0.90, 1.10	0.925
Confidence	1.50	1.08, 2.08	0.016*
Attitudes	0.95	0.70, 1.28	0.727
Perceived Barriers	0.57	0.42, 0.78	<0.0005*

*LogE(Number Structure Activities Completed)$_{i,j}$ = 0.64 – 0.29 Group$_{i,j}$ + 0.30 Time$_{i,j}$ – 0.08 Group*Time$_{i,j}$ – 0.01 Knowledge $_{i,j}$ – 0.05 Intention $_{i,j}$ + 0.41 Confidence $_{i,j}$ – 0.05 Attitudes $_{i,j}$ – 0.56 Perceived Barriers $_{i,j}$*
i=1,2...57; j=1,2; Goodness of fit (QIC)=80.55

$Time_{ij} \begin{cases} 0: O1 \\ 1: O3 \end{cases}$
$Group_{ij} \begin{cases} 0: control \\ 1: intervention \end{cases}$

Model 2 [b,d]			
Parameter[c]	**Exp(β)**	**Exp(95% CI)**	**p-value**
Group (ref=control)	0.75	0.48, 1.18	0.213
Time (ref=O1)	1.37	1.04, 1.79	0.026*
Group*Time	0.98	0.67, 1.43	0.905
Knowledge	0.99	0.98, 1.00	0.066
Intention	0.99	0.89, 1.11	0.910
Confidence Patient	1.17	0.89,1.54	0.272
Confidence Business	1.34	0.99, 1.81	0.059
Attitudes Illicit Misuse	1.24	0.98, 1.57	0.076
Attitudes Rx Misuse	0.67	0.50, 0.91	0.011*
Perceived Barriers Support	0.66	0.49, 0.88	0.005*
Perceived Barriers Business	0.83	0.69, 1.00	0.046*

*LogE(Number Structure Activities Completed)$_{i,j}$ = 1.43 – 0.29 Group$_{i,j}$ + 0.31 Time$_{i,j}$ – 0.02 Group*Time$_{i,j}$ – 0.01 Knowledge $_{i,j}$ – 0.01 Intention $_{i,j}$ + 0.16 Confidence Patient $_{i,j}$ + 0.29 Confidence Business $_{i,j}$ + 0.21 Attitudes Illicit $_{i,j}$ – 0.40 Attitudes Rx $_{i,j}$ – 0.42 Perceived Barriers Support $_{i,j}$ – 0.19 Perceived Barriers Business*
i=1,2...57; j=1,2; Goodness of fit (QIC)=80.426

$Time_{ij} \begin{cases} 0: O1 \\ 1: O3 \end{cases}$
$Group_{ij} \begin{cases} 0: control \\ 1: intervention \end{cases}$

[a]Results of generalized estimating equation (GEE) analyses utilizing a negative binomial distribution with log-link function. Dependent variable=number structure activities completed. Independent variables=Group(intervention, control), Time(O1, O3), Group*Time, knowledge score, intention score, confidence score, attitudes score, perceived barriers score. Significance denoted by *.

[b]Statistically significant covariates opioid-specific prescription volume and sex were retained in the model.

[c]Reference level: Group=control, Time=O1.

[d]Results of generalized estimating equation (GEE) analyses utilizing a negative binomial distribution with log-link function. Dependent variable=number structure activities completed. Independent variables=Group(intervention, control), Time(O1, O3), Group*Time, knowledge score, intention score, confidence regarding patient- and business-oriented activities scores, attitudes regarding illicit and prescription opioid misuse scores, perceived barriers related to support/resources and business logistics scores. Significance denoted by *.

4.2.4.2 Number of Process Activities Engaged

Hypothesis H10a stated that knowledge, intention, and beliefs (perceived barriers, attitudes, confidence) will be associated with number of naloxone service process activities engaged in across 3 months. In regression analyses, two models were examined to assess potential differences in effect based on overall/aggregate scale predictors (Model 1) versus detailed scale predictors (Model 2). In Model 1, respondent confidence scores were positively associated and perceived attitude scores were negatively associated with the number of naloxone service process activities engaged in among intervention and control pharmacies from O1 to O3 (Table 4.42). Specifically, the number of process activities engaged in was 1.43 higher and 0.77 lower for every 1-point increase in confidence ($p<0.0005$) and perceived attitudes ($p=0.015$) scores, respectively. Participant and practice-level characteristics were controlled for, including: sex, race, and years practicing pharmacy (participant-level); and prescription volume, opioid-specific prescription volume, pharmacy type, and rurality (practice-level). Only statistically significant covariates were retained in the final model. Pharmacist knowledge about naloxone, intention to provide naloxone services, and perceived barriers regarding naloxone services were not associated with number of process activities engaged.

When examining detailed sub-scales in Model 2, we found that confidence regarding business-oriented activities scores were positively associated and attitudes regarding illicit opioid misuse scores were negatively associated with the number of naloxone service process activities engaged in among intervention and control pharmacies from O1 to O3. Also, perceived barriers related to support and resources scores and perceived barriers related to business logistics scores showed negative and positive associations with the number of processes, respectively, where higher scores represent more perceived barriers. Specifically, the number of process activities

247

engaged in was 1.30 higher and 0.85 lower for every 1-point increase in confidence regarding business-oriented activities (p=0.007) and attitudes regarding illicit opioid misuse (p=0.012) scores, respectively. Similarly, the number of process activities engaged in was 1.16 higher and 0.84 lower for every 1-point increase in perceived barriers regarding business logistics (p=0.014) and perceived barriers reading support and resources (p=0.040) scores, respectively.

In summary, hypothesis H10a stated that knowledge, intention, and beliefs (perceived barriers, attitudes, confidence) will be associated with number of naloxone service process activities engaged in across 3 months. We failed to reject the null hypothesis, and concluded that knowledge, intention, and beliefs were not all associated with number of process activities engaged.

Table 4.42 Relationship Between Knowledge, Intention, Confidence, and Perceived Barriers with Number of Process Activities Engaged In Over 3 Months (N=57)

Model 1 [a, b]			
Parameter [c]	**Exp(β)**	**Exp(95% CI)**	**p-value**
Group (ref=control)	1.23	0.90, 1.70	0.200
Time (ref=O1)	1.50	1.25, 1.79	<0.0005*
Group*Time	0.84	0.65, 1.09	0.193
Knowledge	1.00	0.99, 1.01	0.830
Intention	1.08	0.96, 1.20	0.209
Confidence	1.43	1.19, 1.71	<0.0005*
Attitudes	0.77	0.63, 0.95	0.015*
Perceived Barriers	0.98	0.84, 1.14	0.807

LogE(Number Process Activities Engaged)$_{i,j}$ = 0.74 + 0.21 Group$_{i,j}$ + 0.40 Time$_{i,j}$ – 0.17 Group*Time$_{i,j}$ – 0.01 Knowledge $_{i,j}$ + 0.07 Intention $_{i,j}$ + 0.36 Confidence $_{i,j}$ – 0.26 Attitudes $_{i,j}$ – 0.02 Perceived Barriers $_{i,j}$
i=1,2...57; j=1,2 ; Goodness of fit (QIC)=50.647

$Time_{ij} \begin{cases} 0: O1 \\ 1: O3 \end{cases}$
$Group_{ij} \begin{cases} 0: control \\ 1: intervention \end{cases}$

Model 2 [b, d]			
Parameter [c]	**Exp(β)**	**Exp(95% CI)**	**p-value**
Group (ref=control)	1.09	0.78, 1.53	0.608
Time (ref=O1)	1.48	1.22, 1.79	<0.0005*
Group*Time	0.92	0.68, 1.25	0.582
Knowledge	1.00	0.99, 1.01	0.845
Intention	1.05	0.94, 1.17	0.383
Confidence Patient	1.13	0.99, 1.29	0.071
Confidence Business	1.30	1.07, 1.57	0.007*
Attitudes Illicit Misuse	0.85	0.75, 0.97	0.012*
Attitudes Rx Misuse	0.87	0.71, 1.07	0.178
Perceived Barriers Support	0.84	0.71, 0.99	0.040*
Perceived Barriers Business	1.16	1.03, 1.30	0.014*

LogE(Number Process Activities Engaged)$_{i,j}$ = 0.81 + 0.09 Group$_{i,j}$ + 0.39 Time$_{i,j}$ – 0.09 Group*Time$_{i,j}$ – 0.001 Knowledge $_{i,j}$ + 0.05 Intention $_{i,j}$ + 0.12 Confidence Patient $_{i,j}$ + 0.26 Confidence Business $_{i,j}$ – 0.16 Attitudes Illicit $_{i,j}$ – 0.14 Attitudes Rx $_{i,j}$ – 0.18 Perceived Barriers Support $_{i,j}$ + 0.15 Perceived Barriers Business
i=1,2...57; j=1,2 ; Goodness of fit (QIC)=49.412

$Time_{ij} \begin{cases} 0: O1 \\ 1: O3 \end{cases}$
$Group_{ij} \begin{cases} 0: control \\ 1: intervention \end{cases}$

[a]Results of generalized estimating equation (GEE) analyses utilizing a negative binomial distribution with log-link function. Dependent variable=number process activities engaged in. Independent variables=Group(intervention, control), Time(O1, O3), Group*Time, knowledge score, intention score, confidence score, attitudes score, perceived barriers score. Significance denoted by *.
[b]Statistically significant covariates prescription volume and opioid-specific prescription volume were retained in the model.
[c]Reference level: Group=control, Time=O1.
[d]Results of generalized estimating equation (GEE) analyses utilizing a negative binomial distribution with log-link function. Dependent variable=number process activities engaged in. Independent variables=Group(intervention, control), Time(O1, O3), Group*Time, knowledge score, intention score, confidence regarding patient- and business-oriented activities scores, attitudes regarding illicit and prescription opioid misuse scores, perceived barriers related to support/resources and business logistics scores. Significance denoted by *.

4.2.4.3 Number of Naloxone Prescriptions Dispensed

Hypothesis H11a stated that knowledge, intention, and beliefs (perceived barriers, attitudes, confidence) will be associated with number of naloxone prescriptions dispensed across 3 months. In regression analyses, two models were examined to assess potential differences in effect based on overall/aggregate scale predictors (Model 1) versus detailed scale predictors (Model 2). In Model 1, results showed that respondent confidence score was positively associated and perceived barriers score was negatively associated with the number of naloxone prescriptions dispensed among intervention and control pharmacies from O1 to O3 (Table 4.43). Specifically, the number of naloxone prescriptions dispensed was 1.46 higher and 0.75 lower for every 1-point increase in confidence score (p=0.031) and perceived barriers score (p=0.022), respectively. Participant and practice-level characteristics were controlled for, including: sex, race, and years practicing pharmacy (participant-level); and prescription volume, opioid-specific prescription volume, pharmacy type, and rurality (practice-level). Only statistically significant covariates were retained in the final model. Pharmacist knowledge about naloxone, intention to provide naloxone services, and attitudes regarding naloxone services implementation were not associated with number of naloxone prescriptions dispensed.

When examining detailed sub-scales in Model 2, results showed that respondent perceived barriers regarding support and resources score was negatively associated with the number of naloxone prescriptions dispensed among intervention and control pharmacies from O1 to O3. Specifically, the number of naloxone prescriptions dispensed was 0.66 lower for every 1-point increase in perceived barriers regarding support and resources score (p=0.005).

In summary, hypothesis H11a stated that knowledge, intention, and beliefs (perceived barriers, attitudes, confidence) will be associated with number of naloxone prescriptions

dispensed across 3 months. We failed to reject the null hypothesis, and concluded that

knowledge, intention, and beliefs are not all associated with number of naloxone prescriptions

dispensed.

Table 4.43 Relationship Between Knowledge, Intention, Confidence, and Perceived Barriers with Number of Naloxone Prescriptions Dispensed Over 3 Months (N=57)

Model 1 [a,b]			
Parameter[c]	**Exp(β)**	**Exp(95% CI)**	**p-value**
Group (ref=control)	1.75	1.04, 2.92	0.034*
Time (ref=O1)	1.14	0.73, 1.81	0.552
Group*Time	1.29	0.71, 2.34	0.400
Knowledge	0.99	0.98, 1.01	0.198
Intention	0.95	0.79, 1.15	0.594
Confidence	1.46	1.04, 2.05	0.031*
Attitudes	0.98	0.67, 1.45	0.935
Perceived Barriers	0.75	0.58, 0.96	0.022*

LogE(Number Process Activities Engaged)$_{i,j}$ = -0.86 + 0.56 Group$_{i,j}$ + 0.14 Time$_{i,j}$ – 0.26 Group*Time$_{i,j}$ – 0.01 Knowledge $_{i,j}$ – 0.05 Intention $_{i,j}$ + 0.38 Confidence $_{i,j}$ – 0.02 Attitudes $_{i,j}$ – 0.29 Perceived Barriers $_{i,j}$
i=1,2...57; j=1,2; Goodness of fit (QIC)=120.847

$$Time_{ij} \begin{cases} 0: O1 \\ 1: O3 \end{cases}$$
$$Group_{ij} \begin{cases} 0: control \\ 1: intervention \end{cases}$$

Model 2 [b,d]			
Parameter[c]	**Exp(β)**	**Exp(95% CI)**	**p-value**
Group (ref=control)	1.56	0.90, 2.71	0.111
Time (ref=O1)	1.14	0.68, 1.91	0.628
Group*Time	1.41	0.73, 2.72	0.307
Knowledge	0.99	0.98, 1.00	0.178
Intention	0.91	0.75, 1.12	0.375
Confidence Patient	1.20	0.93, 1.55	0.170
Confidence Business	1.20	0.79, 1.84	0.396
Attitudes Illicit Misuse	0.87	0.60, 1.25	0.443
Attitudes Rx Misuse	1.13	0.79, 1.62	0.515
Perceived Barriers Support	0.66	0.49, 0.88	0.005*
Perceived Barriers Business	1.11	0.93, 1.33	0.261

LogE(Number Process Activities Engaged)$_{i,j}$ = -0.73 + 0.45 Group$_{i,j}$ + 0.13 Time$_{i,j}$ + 0.34 Group*Time$_{i,j}$ – 0.01 Knowledge $_{i,j}$ – 0.09 Intention $_{i,j}$ + 0.18 Confidence Patient $_{i,j}$ + 0.18 Confidence Business $_{i,j}$ – 0.14 Attitudes Illicit $_{i,j}$ + 0.12 Attitudes Rx $_{i,j}$ – 0.42 Perceived Barriers Support $_{i,j}$ + 0.11 Perceived Barriers Business
i=1,2...57; j=1,2; Goodness of fit (QIC)=123.421

$$Time_{ij} \begin{cases} 0: O1 \\ 1: O3 \end{cases}$$
$$Group_{ij} \begin{cases} 0: control \\ 1: intervention \end{cases}$$

[a]Results of generalized estimating equation (GEE) analyses utilizing a negative binomial distribution with log-link function. Dependent variable=number naloxone prescriptions. Independent variables=Group(intervention, control), Time(O1, O3), Group*Time, knowledge score, intention score, confidence score, attitudes score, perceived barriers score. Significance denoted by *.
[b]Statistically significant covariate prescription volume was retained in the model.
[c]Reference level: Group=control, Time=O1.
[d]Results of generalized estimating equation (GEE) analyses utilizing a negative binomial distribution with log-link function. Dependent variable=number naloxone prescriptions dispensed. Independent variables=Group(intervention, control), Time(O1, O3), Group*Time, knowledge score, intention score, confidence regarding patient- and business-oriented activities scores, attitudes regarding illicit and prescription opioid misuse scores, perceived barriers related to support/resources and business logistics scores. Significance denoted by *.

4.2.5 Motivation Factors

Hypothesis 12a stated that economic gains and social gains (versus losses), as well as opportunity framing (versus threat framing) will be associated with intention to dispense naloxone or perform naloxone services, as measured at baseline. To assess this, motivation to participate in pharmacy-based naloxone services was measured at baseline. The overall motivation scale had high internal consistency (Cronbach's alpha=0.832). A priori scale categories based on Kennedy and Fiss' Motivations for Adopting Innovation Model all had moderate to high internal consistency, including: Economic Gains (Cronbach's alpha=0.824); Economic Losses (Cronbach's alpha= 0.733; Social Gains (Cronbach's alpha=0.790); Social Losses (Cronbach's alpha=0.618); Technical Efficacy (Cronbach's alpha=0.867); Social Legitimacy (Cronbach's alpha=0.748); Opportunity Framing (Cronbach's alpha=0.721); and Threat Framing (Cronbach's alpha=0.719). One scale item that reduced internal consistency for the Economic Losses construct was removed (see Appendix K). Respondent motivations at O1 are described below in terms of frequency of agreement or disagreement to scale items (Table 4.44).

Table 4.44 Frequency of Respondents' Motivations for Participating in Pharmacy-Based Naloxone Services at O1 (N=64)

Question [a]	n (%) [b]		
	All (N=64)	Control (N=32)	Intervention (N=32)
Social Gains			
Being perceived as a pharmacy leader			
Strongly disagree	2 (3.2)	0	2 (6.5)
Disagree	2 (3.2)	2 (6.5)	0
Somewhat disagree	2 (3.2)	1 (3.2)	1 (3.2)
Neither agree nor disagree	7 (11.3)	5 (16.1)	2 (6.5)
Somewhat agree	13 (21.0)	2 (6.5)	**11 (35.5)**
Agree	**20 (32.3)**	**13 (41.9)**	7 (22.6)
Strongly agree	16 (25.8)	8 (25.8)	8 (25.8)
Advancing the profession of pharmacy			
Strongly disagree	0	0	0
Disagree	1 (1.6)	1 (3.2)	0
Somewhat disagree	2 (3.2)	0	2 (6.5)
Neither agree nor disagree	2 (3.2)	1 (3.2)	1 (3.2)
Somewhat agree	10 (16.1)	5 (16.1)	5 (16.1)
Agree	**27 (43.5)**	**13 (41.9)**	**14 (45.2)**
Strongly agree	20 (32.3)	11 (35.5)	9 (29.0)
Improving the image of my pharmacy in the community			
Strongly disagree	2 (3.2)	1 (3.2)	1 (3.2)
Disagree	1 (1.6)	1 (3.2)	0
Somewhat disagree	0	0	0
Neither agree nor disagree	12 (19.4)	6 (19.4)	6 (19.4)
Somewhat agree	11 (17.7)	4 (12.9)	7 (22.6)
Agree	**22 (35.5)**	**13 (41.9)**	**9 (29.0)**
Strongly agree	14 (22.6)	6 (19.4)	8 (25.8)
Fulfilling my duty and obligation as a pharmacist to help patients			
Strongly disagree	0	0	0
Disagree	0	0	0
Somewhat disagree	1 (1.6)	0	1 (3.2)
Neither agree nor disagree	1 (1.6)	1 (3.2)	0
Somewhat agree	5 (8.1)	2 (6.5)	3 (9.7)
Agree	24 (38.7)	**14 (45.2)**	10 (32.3)
Strongly agree	**31 (50.0)**	**14 (45.2)**	**17 (54.8)**

Improving the health and well-being of my patients			
Strongly disagree	0	0	0
Disagree	0	0	0
Somewhat disagree	0	0	0
Neither agree nor disagree	1 (1.8)	1 (3.2)	0
Somewhat agree	9 (14.5)	3 (9.7)	6 (19.4)
Agree	24 (38.7)	**15 (48.4)**	9 (29.0)
Strongly agree	**28 (45.2)**	12 (38.7)	**16 (51.6)**
Social Losses			
Preventing possible opioid overdose deaths in my community			
Strongly disagree	0	0	0
Disagree	0	0	0
Somewhat disagree	1 (1.6)	0	1 (3.2)
Neither agree nor disagree	1 (1.6)	1 (3.2)	0
Somewhat agree	6 (9.7)	2 (6.5)	4 (12.9)
Agree	22 (35.5)	12 (38.7)	10 (32.3)
Strongly agree	**32 (51.6)**	**16 (51.6)**	**16 (51.6)**
Avoiding losing the status and respect of my professional peers			
Strongly disagree	10 (16.1)	4 (12.9)	6 (19.4)
Disagree	11 (17.7)	5 (16.1)	6 (19.4)
Somewhat disagree	4 (6.5)	2 (6.5)	2 (6.5)
Neither agree nor disagree	**18 (29.0)**	**10 (32.3)**	**8 (25.8)**
Somewhat agree	8 (12.9)	3 (9.7)	5 (16.1)
Agree	8 (12.9)	6 (19.4)	2 (6.5)
Strongly agree	3 (4.8)	1 (3.2)	2 (6.5)
Avoiding being perceived as an uncompassionate and uncaring organization			
Strongly disagree	8 (12.9)	4 (12.9)	4 (12.9)
Disagree	10 (16.1)	4 (12.9)	**6 (19.4)**
Somewhat disagree	3 (4.8)	2 (6.5)	1 (3.2)
Neither agree nor disagree	**15 (24.2)**	**10 (32.3)**	5 (16.1)
Somewhat agree	8 (12.9)	2 (6.5)	**6 (19.4)**
Agree	14 (22.6)	8 (25.8)	**6 (19.4)**
Strongly agree	4 (6.5)	1 (3.2)	3 (9.7)
Avoiding harm to my patients			
Strongly disagree	1 (1.6)	0	1 (3.2)
Disagree	1 (1.6)	1 (3.2)	0
Somewhat disagree	0	0	0
Neither agree nor disagree	5 (8.1)	3 (9.7)	2 (6.5)

Somewhat agree	7 (11.3)	3 (9.7)	4 (12.9)
Agree	**26 (41.9)**	**14 (45.2)**	**12 (38.7)**
Strongly agree	22 (35.5)	10 (32.3)	**12 (38.7)**
Economic Losses			
Complying with a professional manager or decision-maker's request [c]			
Strongly disagree	9 (14.5)	4 (12.9)	5 (16.1)
Disagree	6 (9.7)	1 (3.2)	5 (16.1)
Somewhat disagree	0	0	0
Neither agree nor disagree	14 (22.6)	8 (25.8)	6 (19.4)
Somewhat agree	4 (6.5)	1 (3.2)	3 (9.7)
Agree	**19 (30.6)**	**14 (45.2)**	5 (16.1)
Strongly agree	10 (16.1)	3 (9.7)	**7 (22.6)**
Avoiding potential loss of patients to pharmacy competitors			
Strongly disagree	10 (16.1)	4 (12.9)	6 (19.4)
Disagree	15 (24.2)	7 (22.6)	**8 (25.8)**
Somewhat disagree	1 (1.6)	1 (3.2)	0
Neither agree nor disagree	**17 (27.4)**	**12 (38.7)**	5 (16.1)
Somewhat agree	6 (9.7)	2 (6.5)	4 (12.9)
Agree	11 (3.2)	4 (12.9)	7 (22.6)
Strongly agree	2 (3.2)	1 (3.2)	1 (3.2)
Avoiding future economic repercussions related to patient overdose			
Strongly disagree	10 (16.1)	4 (12.9)	6 (19.4)
Disagree	10 (16.1)	4 (12.9)	6 (19.4)
Somewhat disagree	1 (1.6)	0	1 (3.2)
Neither agree nor disagree	**16 (25.8)**	**11 (35.5)**	5 (16.1)
Somewhat agree	6 (9.7)	3 (9.7)	3 (9.7)
Agree	14 (22.6)	7 (22.6)	**7 (22.6)**
Strongly agree	5 (8.1)	2 (6.5)	3 (9.7)
Preventing healthcare expenditures related to overdose treatment in my community			
Strongly disagree	0	1 (3.2)	0
Disagree	6 (9.7)	0	5 (16.1)
Somewhat disagree	0	0	0
Neither agree nor disagree	12 (19.4)	**9 (29.0)**	3 (9.7)
Somewhat agree	14 (22.6)	7 (22.6)	7 (22.6)
Agree	**19 (30.6)**	**9 (29.0)**	**10 (32.3)**
Strongly agree	11 (17.7)	5 (16.1)	6 (19.4)
Economic Gains			

Providing an additional revenue stream for my pharmacy			
Strongly disagree	7 (11.3)	2 (6.5)	5 (16.1)
Disagree	5 (8.1)	2 (6.5)	3 (9.7)
Somewhat disagree	4 (6.5)	3 (9.7)	1 (3.2)
Neither agree nor disagree	**16 (25.8)**	**11 (35.5)**	5 (16.1)
Somewhat agree	9 (14.5)	5 (16.1)	4 (12.9)
Agree	**16 (25.8)**	6 (19.4)	**10 (32.3)**
Strongly agree	5 (8.1)	2 (6.5)	3 (9.7)
Providing a competitive advantage over other pharmacies			
Strongly disagree	7 (11.3)	2 (6.5)	5 (16.1)
Disagree	6 (9.7)	4 (12.9)	2 (6.5)
Somewhat disagree	1 (1.6)	1 (3.2)	0
Neither agree nor disagree	16 (25.8)	**9 (29.0)**	7 (22.6)
Somewhat agree	8 (12.9)	5 (16.1)	3 (9.7)
Agree	**17 (27.4)**	7 (22.6)	**10 (32.3)**
Strongly agree	7 (11.3)	3 (9.7)	4 (12.9)
Saving staff time contacting physicians or other providers to prescribe naloxone			
Strongly disagree	7 (11.3)	3 (9.7)	4 (12.9)
Disagree	9 (14.5)	3 (9.7)	6 (19.4)
Somewhat disagree	3 (4.8)	1 (3.2)	2 (6.5)
Neither agree nor disagree	**21 (33.9)**	**12 (38.7)**	**9 (29.0)**
Somewhat agree	9 (14.5)	5 (16.1)	4 (12.9)
Agree	10 (16.1)	6 (19.4)	4 (12.9)
Strongly agree	3 (4.8)	1 (3.2)	2 (6.5)
Improving the technical expertise and job skills of myself / my pharmacy staff			
Strongly disagree	1 (1.6)	1 (32.)	0
Disagree	2 (3.2)	1 (3.2)	1 (3.2)
Somewhat disagree	1 (1.6)	0	1 (3.2)
Neither agree nor disagree	5 (8.1)	3 (9.7)	2 (6.5)
Somewhat agree	16 (25.8)	4 (12.9)	**12 (38.7)**
Agree	**26 (41.9)**	**17 (54.8)**	9 (29.0)
Strongly agree	11 (17.7)	5 (16.1)	6 (19.4)

[a] On a Likert-type scale of 1 to 7, where 1=strongly disagree and 7=strongly agree.

[b] Percentages may differ due to item non-response.

[c] This item was removed due to lower internal consistency.

In order to determine which factors were most influential in motivating respondents to participate in pharmacy-based naloxone services, mean differences between scale scores were assessed (Table 4.45a-b). Higher mean scale scores represent greater motivation. Values are mean (SD) unless stated otherwise. The motivation factor with the highest mean scale score was social gains (5.88 (0.85)), while economic losses had the lowest mean scale score (4.24 (1.43)). There was a statistically significant difference in motivation for economic gains over economic losses (mean difference: 0.32, p=0.021), social gains over social losses (mean difference: 0.90, p<0.0005), social legitimacy over technical efficacy (mean difference: 1.03, p<0.0005), and opportunity framing over threat framing (mean difference: 0.61, p<0.0005).

Table 4.45a Motivation Factor Mean Scale Scores and Internal Consistency at O1 (N=64)

Motivation Factors	Mean (SD)	Cronbach's Alpha
Economic Gains (EG)	4.56 (1.36)	0.824
Economic Loss (EL)	4.24 (1.43)	0.733
Social Gains (SG)	5.88 (0.85)	0.790
Social Loss (SL)	4.98 (1.02)	0.618
Technical Efficacy (TEff) [a]	4.40 (1.28)	0.867
Social Legitimacy (SLeg) [b]	5.43 (0.77)	0.748
Opportunity Framing (OF) [c]	5.22 (0.82)	0.721
Threat Framing (TF) [d]	4.61 (1.02)	0.719
Overall Motivation Scale	5.02 (0.80)	0.832

[a] Technical efficacy = economic gains + economic losses.
[b] Social legitimacy = social gains + social losses.
[c] Opportunity framing = economic gains + social gains.
[d] Threat framing = economic losses + economic gains.

Table 4.45b. Mean Differences in Respondents' Motivation Factor Scale Scores at O1 (N=64)

Motivation Factor	Mean Difference [a,b] p-value							
	EG	EL	SG	SL	TEff	SLeg	OF	TF
EG	-	0.32 0.021	-1.32 <0.0005	-0.42 0.017	N/A	N/A	N/A	N/A
EL		-	-1.65 <0.0005	-0.74 <0.0005	N/A	N/A	N/A	N/A
SG			-	0.90 <0.0005	N/A	N/A	N/A	N/A
SL				-	N/A	N/A	N/A	N/A
TEff					-	-1.03 <0.0005	N/A	N/A
SLeg						-	N/A	N/A
OF							-	0.61 <0.0005
TF								-

[a] Mean differences = row-column
[b] Based on two-sided paired sample t-test with a priori alpha=0.05.

After determining the most influential motivation factors above, regression analyses were performed in order to assess the association of motivation factors including economic gains, economic losses, social gains, social losses, technical efficacy, social legitimacy, opportunity framing, and threat framing with intention to provide naloxone services at O1. Multicollinearity was not detected among predictors (VIF < 10). Respondent economic gains scores and technical efficacy scores were negatively associated with respondent intention to provide pharmacy-based naloxone services at O1 (Table 4.46a-c). Specifically, intention was 0.56 lower for every 1-point increase in economic gains scores (p=0.002) and 0.32 lower for every 1-point increase in technical efficacy scores (p=0.030). Participant and practice-level characteristics were controlled for, including: sex, race, and years practicing pharmacy (participant-level); and prescription volume, opioid-specific prescription volume, pharmacy type, and rurality (practice-level). Economic losses, social gains, social losses, social legitimacy, opportunity framing, and threat

framing motivation factors were not associated with intention to provide naloxone services at baseline.

In summary, hypothesis 12a stated that economic gains and social gains (versus losses), as well as opportunity framing (versus threat framing) will be associated with intention to dispense naloxone or perform naloxone services, as measured at baseline. We failed to reject the null hypothesis, and concluded that economic gains, social gains, and opportunity framing were not all associated with intention at baseline.

Table 4.46a Relationship Between Economic Gains, Economic Losses, Social Gains, Social Losses and Intention at O1 (N=64)[a,b]

Parameter	β	95% CI	p-value
Economic Gains (EG)	-0.56	-0.91, -0.22	0.002*
Economic Losses (EL)	0.21	-0.10, 0.52	0.211
Social Gains (SG)	0.13	-0.27, 0.53	0.515
Social Losses (SL)	0.07	-0.28, 0.42	0.680
$R^2=0.264$, $F=1.569$, $p=0.139$			

[a]Results of multiple linear regression analyses. Dependent variable=intention score. Independent variables=economic gains, economic losses, social gains, social losses. Significance denoted by *.
[b]Controlling for covariates prescription volume, opioid-specific prescription volume, rurality, pharmacy type, sex, race and years in pharmacy practice did not alter model conclusions.

Table 4.46b Relationship Between Technical Efficacy, Social Legitimacy and Intention at O1 (N=64)[a,b]

Parameter	β	95% CI	p-value
Technical Efficacy (TEff)	-0.32	-0.61, -0.03	0.030*
Social Legitimacy (SLeg)	0.19	-0.27, 0.66	0.409
$R^2=0.155$, $F=1.015$, $p=0.441$			

[a]Results of multiple linear regression analyses. Dependent variable=intention score. Independent variables=technical efficacy, social legitimacy. Significance denoted by *.
[b]Controlling for covariates prescription volume, opioid-specific prescription volume, rurality, pharmacy type, sex, race and years in pharmacy practice did not alter model conclusions.

Table 4.46c Relationship Between Opportunity Framing, Threat Framing and Intention at O1 (N=64)[a,b]

Parameter	β	95% CI	p-value
Opportunity Framing (OF)	-0.55	-1.12, 0.02	0.058
Threat Framing (TF)	0.17	-0.30, 0.63	0.488
$R^2=0.147$, $F=0.960$, $p=0.484$			

[a]Results of multiple linear regression analyses. Dependent variable=intention score. Independent variables=opportunity framing, threat framing. Significance denoted by *.
[b]Controlling for covariates prescription volume, opioid-specific prescription volume, rurality, pharmacy type, sex, race and years in pharmacy practice did not alter model conclusions.

4.2.6 Summary of Aim 2 Results

The primary operating hypothesis in Aim 2 was that receipt of a targeted naloxone training program will improve Alabama community pharmacists' knowledge, intentions, attitudes, confidence, perceived barriers, service structure and process implementation, and number of naloxone prescriptions dispensed. Specifically, we found that the EmpoweringCommunityPharmacists training program created and delivered in this study had a statistically significant effect on pharmacists' intention and confidence to provide naloxone services when compared to control. However, while overall confidence was associated with all behavior outcomes, intention was not associated with any behavior outcomes. Implications of this intention-behavior gap are discussed in more detail in the next chapter (Section 5.2). Regarding factors motivating community pharmacists to participate in naloxone services, social gains was the most influential factor, but only economic gains and technical efficacy were associated with intention to provide naloxone services. Support for Aim 2 hypotheses is summarized below (Table 4.47, Figure 4.13).

Table 4.47 Summary of Aim 2 Results and Support for Hypotheses

Hypothesis	Alternative Hypothesis	Outcome
1	Change in naloxone **knowledge** from baseline to post-training and baseline to 3-months will be greater among intervention compared to control group pharmacists	Failed to reject the null
2	Change in **intention** to dispense naloxone or perform naloxone services from baseline to post-training and baseline to 3-months will be greater among intervention compared to control group pharmacists	Rejected the null
3	Change in **attitudes** regarding naloxone services from baseline to post-training and baseline to 3-months will be greater among intervention compared to control group pharmacists	Failed to reject the null
4	Change in **confidence** regarding naloxone services from baseline to post-training and baseline to 3-months will be greater among intervention compared to control group pharmacists	Rejected the null
5	Change in **perceived barriers** regarding naloxone services from baseline to post-training and baseline to 3-months will be greater among intervention compared to control group pharmacists	Failed to reject the null
6	Number of naloxone service **structure** activities completed by the end of the 3-month study period will be greater among intervention compared to control group pharmacists	Failed to reject the null
7	Number of naloxone **process** activities engaged in by the end of the 3-month study period will be greater among intervention compared to control group pharmacists	Failed to reject the null
8	Change in number of **naloxone prescriptions** dispensed from baseline to 3-months will be greater among intervention compared to control group pharmacists	Failed to reject the null
9	**Knowledge, intention, and beliefs** (perceived barriers, attitudes, confidence) will be associated with number of naloxone service **structure** activities completed across 3 months	Failed to reject the null
10	**Knowledge, intention, and beliefs** (perceived barriers, attitudes, confidence) will be associated with number of naloxone service **process** activities engaged in across 3 months	Failed to reject the null
11	**Knowledge, intention, and beliefs** (perceived barriers, attitudes, confidence) will be associated with number of naloxone **prescriptions** dispensed across 3 months	Failed to reject the null
12	**Economic gains** and **social gains** (versus losses), as well as **opportunity framing** (versus threat framing) will be associated with intention to dispense naloxone or perform naloxone services, as measured at baseline	Failed to reject the null
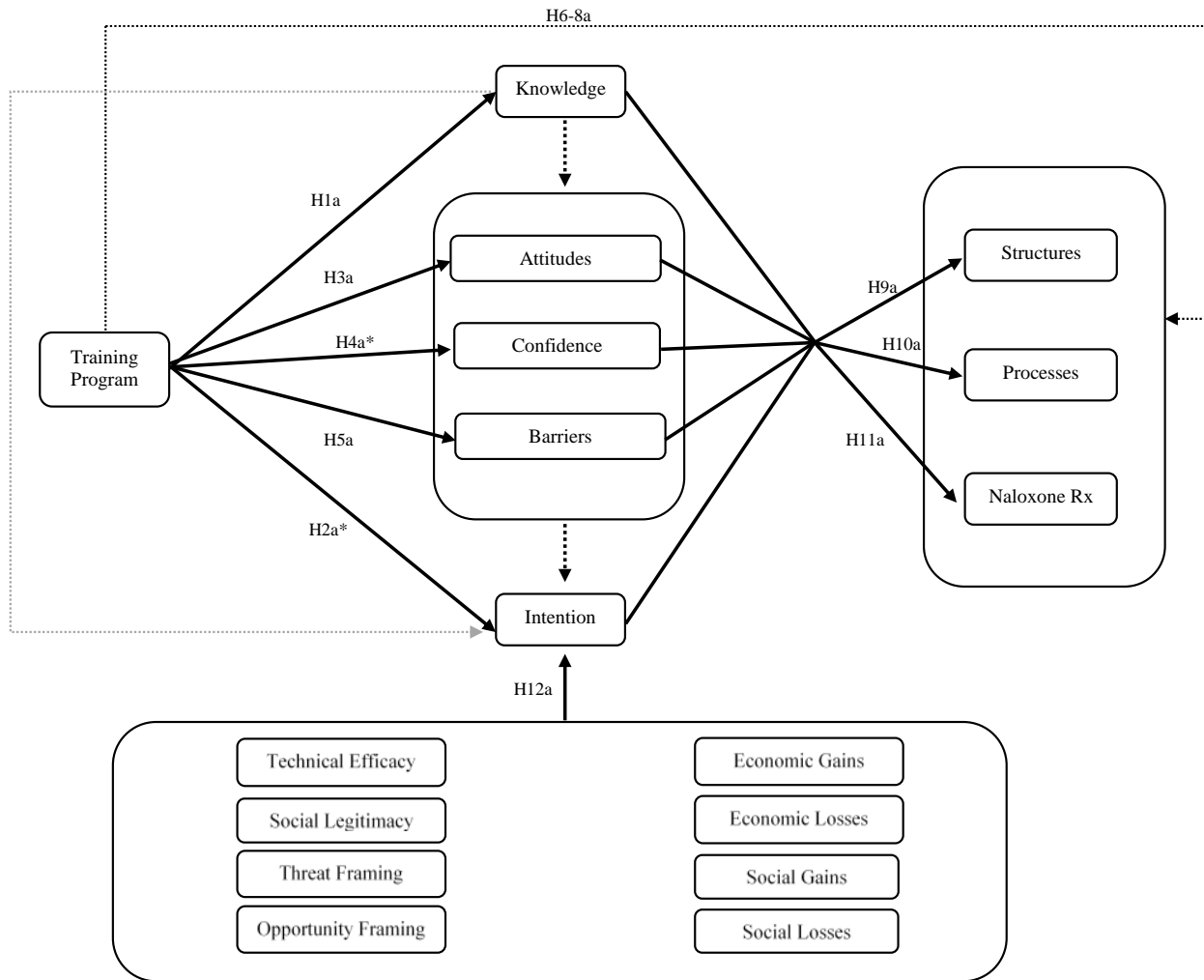
Figure 4.13 Support for Aim 2 Hypotheses. Hypotheses for the which the null were rejected are indicated by *.

Chapter 5. Discussion

This multi-phase mixed methods study was conducted over a 3-month time frame with the goal to enhance naloxone services implementation in community pharmacies in Alabama. In order to achieve this, two aims were conducted: 1) to incorporate community pharmacists' training needs and experts' strategies to overcome barriers regarding pharmacy-based naloxone services implementation into the development of a targeted training program in Alabama; and 2) to evaluate a targeted naloxone training program among community pharmacists in Alabama. Both aims were successfully completed.

5.1 Aim 1 Summary and Implications

In Aim 1, 10 community pharmacists were interviewed to explore community pharmacists' naloxone training needs in terms of content and format, as well as attitudes and barriers to pharmacy-based naloxone services implementation. Findings from interviews revealed that, although pharmacists generally were supportive of pharmacy-based naloxone services, they needed more training regarding basic naloxone facts and dispensing legalities in Alabama, such as where to find Alabama's statewide standing naloxone order and how to use the standing order in practice. They were also uncomfortable and lacked training in how to approach and communicate with patients about their potential opioid overdose risk and need for naloxone, and especially methods to overcome perceived patient resistance to receiving naloxone. These individual-level barriers were more commonly discussed than organization-level or external-level barriers, in which pharmacists cited lack of time and insurance coverage issues as major barriers, respectively. This is similar to findings from other studies, which found that perceived need for additional training, lack of strategies for communicating with or identifying patients,

stigma, lack of time, and cost-related issues were the major barriers pharmacists faced in providing naloxone services.[294-296] Additionally, in reference to this particular topic of naloxone services, they also preferred live, interactive or hands-on education like in-person sessions or live webinars as opposed to static or passive formats like paper-based or online home-study modules. This is similar to opinions found in other studies regarding the format of educational materials.[40,228,267] However, in order for these training needs, attitudes, and barriers to be put into context and to inform development of the most relevant and useful training program, it was also necessary to understand community pharmacists' current naloxone services implementation strategies.

Interviews also helped us to explore Alabama community pharmacists' current naloxone services implementation strategies. We found that pharmacists had successfully employed several strategies, including integration of naloxone services into the regular prescription dispensing workflow by using reminder aids like stickers in prescription bags to alert the pharmacist to opioid and naloxone counseling opportunities. This is similar to strategies used in other pharmacy-based services, such as immunization services, in which age- or medication-related medication profile reviews and reminder aids in prescription bags have been used to alert the pharmacist to counseling opportunities.[37,297]

Pharmacists also discussed using a wait-and-see approach (subsequent to a physician's prescription or patient request) more often than a proactive approach (self-initiated) to engage and interact with patients when recommending naloxone. This may be due to pharmacists' discomfort with approaching and communicating with patients about their opioid overdose risk and need for naloxone. As mentioned above, interviews revealed that pharmacists were not confident in recommending naloxone because they felt as if they were targeting patients and

265

perceived that patients would be resistant. This is consistent with views that have been found in previous research.[173,182,295]

Furthermore, pharmacists more often utilized a targeted approach (based on specific opioid dose or patient characteristics) rather than a universal approach (any patient, any opioid, any dose) to identify patients to whom they could recommend naloxone. This may be due to pharmacists' pressure to comply with corporate culture or organization-level policies and procedures related to opioid and naloxone dispensing, as well as state and federal guidelines and regulations, which were two factors discussed during pharmacist interviews.[298] In particular, this targeted approach may be influenced by the external culture of stigma and sensationalism surrounding the "opioid crisis," especially in light of recent articles and publications in the news highlighting the CDC's Opioid Prescribing Guidelines and the higher risk of opioid overdose at doses $\geq$50 MMEs or in patients with certain conditions like COPD that put them at higher risk of opioid-related respiratory depression.[299] However, after learning what was being done by pharmacists, it was necessary to understand the best practices and strategies recommended by individuals with clinical and/or pedagogical expertise in opioids for pain management, opioid use disorder, and naloxone.

In addition to what was learned from Alabama community pharmacists, 6 opioid/naloxone experts from throughout the U.S. were interviewed to explore recommended strategies for overcoming barriers to community pharmacy-based naloxone services implementation. Experts recommended creating a normative culture of safety in the pharmacy through three means: using safety-centered marketing materials and communication; using a universal rather than targeted approach; and "closing the loop." First, experts recommended using safety-centered marketing materials and communication, which aligned well with current

marketing and communication strategies currently employed by interviewed pharmacists. By using sensitive language, elements of motivational interviewing (MI) like rolling with resistance, and safety-centered phrases (e.g. *"Think of naloxone like an Epi-pen®"*) when communicating, whether via written means like in-store posters or verbal means like in-person prescription consultations, a normative culture is created that reduces stigma towards people seeking or receiving naloxone.[48,300] However, while pharmacists discussed using in-store advertising like flyers and prescription bag stuffers to advertise their naloxone service, experts recommended expanding marketing efforts to include external media like TV, radio, and print advertisements.

Next, experts also recommended using a universal rather than a targeted approach to identify patients to whom they could recommend naloxone. This is in contrast to pharmacists' current strategies, with pharmacists more often discussing use of the targeted approach compared to the universal approach. Although the targeted approach may be more cost effective in terms of not dispensing naloxone to people who are at lower risk of opioid overdose and have less chance of needing to use the naloxone, the universal approach is more time-efficient in the busy community pharmacy setting as it reduces staff time screening for opioid overdose risk. The universal approach also reduces issues of perceived stereotyping, and may thus lower patient resistance to receiving naloxone and overcome pharmacists' discomfort with making the recommendation.[48,219,300,301] In addition to this, the universal approach offers benefit to public health over the targeted approach, as it has the potential to reduce deaths resulting from accidental prescription opioid exposure in children or other individuals in the home other than the person for whom the opioid was prescribed.

Lastly, experts stressed the importance of "closing the loop" by following up with both patients and providers after dispensing naloxone, thereby building a trusting relationship between

all parties in the healthcare process. In particular, experts recommended that pharmacists follow-up with prescribers after dispensing naloxone as a best practice, but pharmacists did not discuss using this strategy. This is similar to practices employed in other clinical pharmacy services, such as MTM and immunization services, in which pharmacist-prescriber reporting is considered a best practice and in some states is even mandated by law.[241,290] Similarly, experts recommended that pharmacists create a two-way referral system by referring patients to alternative sources to obtain naloxone when it is not in stock in the pharmacy, but also establishing a relationship with a local prescriber to let them know that the pharmacy can serve as a source for prescribers to refer patients in need of naloxone. This relationship can be initiated or maintained through personal selling, a communication strategy recommended by experts and discussed by some pharmacists during interviews. Personal selling, as well as academic detailing, a related concept involving personalized recommendations and in-person interactions, have been used to successfully promote healthcare provider uptake of services.[302-304] Indeed, this personal touch recommended by experts is in contrast to the centralization of processes or use of a central call center to identify and contact individuals that was a strategy used by some interviewed pharmacists. This centralization can reduce in-store task burden and be time-efficient for the pharmacist, but results in less buy-in from the patient due to the lack of personalized recommendations from their familiar local pharmacist.[304-306] On the other hand, the personalized, two-way referral process discussed by experts is similar to the medical home or coordinated care system in which in which a patient has a team of healthcare providers working on their behalf, thus ensuring that no patient falls through the cracks.[307,308] There is opportunity for this concept to be expanded into a coordinated "opioid safety network" between pharmacists, prescribers, treatment facilities, and other healthcare providers in future studies.

Overall, experts' recommendations discussed above represent priority areas for action for pharmacists to enhance implementation of naloxone services in their pharmacies. Accordingly, these recommended strategies, along with interviewed pharmacists' self-reported training needs, were taken into account in the development of the finalized EmpoweringCommunityPharmacists training program. To create the most feasible, acceptable, and useful training program, stakeholder panel feedback was sought and the training program was modified over two iterative rounds. Panel feedback primarily addressed additions and deletions of content based on literature recommended by experts, as well as re-organization of the format to include more figures and tables and less verbose text. Expert speakers were also recruited from amongst specialized content experts in order to increase the credibility of the continuing education program. In particular, the majority of panel members agreed or strongly agreed that they were satisfied with the information presented in each module and that it was useful for practicing Alabama community pharmacists. This is consistent with research showing that a participatory design approach is effective at creating relevant and feasible training programs for the end-user.[27,309]

However, despite the usefulness of the stakeholder panel in fine-tuning and ensuring the validity of the training materials, several lessons were learned and there was room for improvement in this process. Specifically, it was challenging to obtain feedback from all pharmacists (end-users) and opioid/naloxone experts in enough time to make modifications based on feedback and then send the modified materials to the same panel members again for a second round of review. In fact, it took approximately one full month for the first round of feedback on training materials to be reviewed and feedback obtained from all pharmacist and general opioid/naloxone experts. Therefore, in order to stay on track with the timing of the

269

study, the modified materials were sent directly to the specialized content experts for the second round of review via in-person or email/videoconference feedback, skipping the planned second round of review amongst end-users and general opioid/naloxone experts using the online feedback questionnaire. Because of this, panelists' ratings on the feedback questionnaire regarding the initial training materials were not able to be compared to ratings after the materials were modified. In future, perhaps additional panel members could be recruited to review smaller portions of training materials, therefore allowing for a quicker turn-around time and additional rounds of review amongst the same group of panelists. Based on this experience, planning for at least 3 rounds of iterative feedback and modification with a pool of more than 10 panelists would be helpful in case some panelists are not able to meet the turn-around time for review. However, the 2-round iterative feedback and review process amongst end-users, general experts, and specialized content experts used in this study was effective in providing guidance to the PI in finalizing the training program.

The final training program was composed of 3 modules: 1) naloxone basics and Alabama legalities; 2) naloxone service implementation strategies; and 3) communication strategies. The EmpoweringCommunityPharmacists training program was similar to existing training program in that it presented information regarding basic naloxone facts, including pharmacology and a review of dosage form, as well as state-specific legalities.[22,196-201] On the other hand, the training program in the current study differed from other existing programs in that it incorporated heretofore unknown Alabama community pharmacists' self-reported naloxone training needs. Previous training programs had not incorporated these self-reported training needs.[22,196-201] Furthermore, the program discussed practical, evidence-based service implementation strategies, including choosing a champion, setting goals, creating a protocol for the service, and setting staff

member roles and tasks using tools like the Gantt chart.[32,117,199,216] These practical tips and tools were lacking in other programs.[32,117,199,216] This study's program also focused on providing communication strategies and "Go To" phrases for use in the community pharmacy setting when discussing opioid overdose risk and the need for naloxone, presented by an expert in motivational interviewing and substance use disorder provider-patient interactions. This focus on communication strategies was of particular need amongst interviewed pharmacists but was lacking in most existing naloxone training programs. [22,32,117,196-201,216] Importantly, the training program was not only knowledge-based, but incorporated skills practice and tools for routinization, including a virtual naloxone administration workshop where attendees of the live online webinar could follow along to a pre-recorded video and practice using Narcan® and Evzio® devices (training devices were mailed to study participants ahead of time), links to tools like prescriber communication faxes and opioid overdose risk assessment screening tools, plus a live role play scenario and communication strategy demonstration by the expert speaker. The impact of this training program was assessed in the second aim of the study.

5.2 Aim 2 Summary and Implications

The finalized naloxone training program described above was delivered in the second phase of the study, with the goal to evaluate the impact of the training program among community pharmacists in Alabama. The training program had a statistically significant effect in increasing pharmacists' intention and confidence in providing naloxone services. Specifically, overall confidence and confidence regarding performing business-oriented activities (stocking naloxone, etc) increased pre (O1) to post (O2), but confidence regarding performing patient-oriented activities (approaching a patient to talk about naloxone, etc) showed an increasing trend

from pre to post in the intervention group, but the change was not statistically significant

compared to control. No significant declines were seen in the intervention group for any

outcome measure from post (O2) to 3-month follow-up (O3), meaning that the effects of the

intervention were sustained over 3 months. However, although hypotheses regarding intention

and confidence were supported, others were not.

We failed to reject the null hypotheses regarding changes in knowledge about naloxone,

attitudes regarding pharmacy-based naloxone services, and perceived barriers to implementation

of pharmacy-based naloxone services. Although increases in knowledge, overall attitudes, and

attitudes related to prescription opioid misuse showed statistically significant increases from pre

to 3 months within the intervention group, there was no significant difference compared to

control. Interestingly, attitudes related to illicit opioid misuse showed no significant change

within either group. Similarly, overall perceived barriers, as well as perceived barriers related to

support and resources and business logistics, showed statistically significant decreases within the

intervention group, but not when compared to control.

Furthermore, we failed to reject the null hypotheses regarding changes in naloxone

service implementation behaviors. Specifically, although the total number of naloxone

prescriptions dispensed showed a statistically significant increase from pre to 3 months within

the intervention group, this change was not significant compared to control. A similar pattern

was seen for naloxone service structure activity completion scores and process activity

engagement scores, with statistically significant increases from pre to 3 months in the

intervention group, but no statistically significant change compared to control. Likewise, no

statistically significant differences were found in the number of structure activities completed,

272

process activities engaged in, or level of structure or process implementation between intervention and control at the end of the 3-month study period.

The fact that changes within the intervention group were not significant when compared to control for many outcome measures may be explained by several issues. First, although the training program was delayed until after the study period for the control group, an increasing trend in knowledge score, while statistically insignificant, was seen within the control group during the 3-month study period. This may have been a result of several factors. The first was the carry-over effect, with control group participants performing better upon re-test because they familiarized themselves with the questions/topic in the interim. Next, a history bias, or influence of concurrent events outside of the study intervention, such as other education programs or media coverage related to opioids and naloxone, may have likewise led to improvement in control group knowledge as well as other belief and behavior measures. Furthermore, simply being enrolled in the current study may have caused control group participants to act in a more favorable manner than normal, otherwise known as the Hawthorne effect. In addition to this, interim email contacts at one and two months post-training, in which intervention participants were provided with recent published articles related to opioids plus naloxone service implementation resources while control participants were provided with articles only, were intended to serve as a reminder or nudge to enhance participant retention. However, interim contacts may also have served as a nudge to change naloxone service implementation behaviors within the control group. Overall, these issues may have diluted the observed impact of the intervention. Associations between outcome measures were also explored to shed some light onto study findings.

Overall confidence was found to be positively associated with number of naloxone prescriptions dispensed, number of structure activities completed, and number of process activities engaged in. Perceived barriers to implementation were also negatively associated with number of naloxone prescriptions dispensed and number of structure activities completed. These findings are consistent with previous studies showing that greater confidence is associated with increased implementation of MTM services in community pharmacies.[232,310] Perceived barriers, particularly individual- and organization-level barriers like patient/provider resistance to recommendations and lack of management/mentor support, have also been shown to inhibit implementation of advanced pharmacy practice.[310,311] Indeed, the influence of confidence and perceived barriers on behaviors aligns with the concept of Reciprocal Determinism, the central tenet of Social Cognitive Theory, which states that behavior (naloxone service implementation) is influenced by personal factors (confidence/self-efficacy and perceived individual-level barriers) and environmental factors (perceived organizational and external barriers).[312,313] However, in addition to confidence and perceived barriers, attitudes also play a role in behavior change.

Interestingly, in the current study, more positive overall attitudes regarding naloxone services were negatively associated with the number of process activities engaged in. This finding is a bit difficult to explain, but may reflect discrepancies between pharmacists' attitudes towards prescription versus illicit opioid misuse and the clientele frequenting the pharmacy, which was not the focus of the current study. The training program in the current study focused on providing naloxone to individuals with prescription opioid misuse. Future studies should explore pharmacists' attitudes towards prescription versus illicit opioid misuse and create targeted education and "Go To" phrases to aid communication in both situations.

Furthermore, contrary to findings from other studies and the Theory of Planned Behavior, which states that intention is the greatest predictor of behavior change, no associations were found between intention and any of the behavior outcomes in this study.[314,315] This intention-behavior gap may be explained by several factors. One reason may be that unanticipated barriers were encountered in the implementation of naloxone services, so that intention was not able to be actualized. Furthermore, if pharmacists were not the decision-makers in their organization, they may not have had control over initiating or enhancing naloxone services, no matter their intention.[310] This type of organization-level barrier has been difficult to overcome in previous studies, and may require longer than three months to gain decision-maker approval and alter organization-wide structures.[316,317] A longer study time frame may be needed to explore effects of intention on behaviors in the long-term.

The training program in the current study was not effective at decreasing perceived barriers to naloxone implementation compared to control, indicating that unmeasured barriers may not have been addressed by training program content. This may be one reason to explain why no significant changes in structure activity implementation were found between intervention and control groups. Therefore, future studies should focus on increasing confidence and decreasing perceived barriers to implementation of naloxone services. The EmpoweringCommunityPharmacists training program, which was effective at increasing confidence, could be built upon to help strengthen its effect on decreasing perceived barriers to implementation. This could be done by expanding the audience and targeting a separate presentation to pharmacy owners, pharmacy managers, and corporate-level managers focusing on how to choose a champion, create a pharmacy protocol for providing naloxone, and assigning staff roles using tools like the Gantt chart.[180,245,318] This would increase buy-in at the pharmacy

level and provide a venue for continuous reinforcement of implementation. For community pharmacists, the training program's content could further focus on decreasing perceived barriers to implementation by incorporating more content related to the role of pharmacy technicians in naloxone services, how to gain management and co-worker support, and how to form collaborative relationships with prescribers for performing opioid counseling and naloxone services.[319,320]

Lastly, motivation factors for participating in naloxone services were explored in order to inform future program uptake. We found that social gains was the most motivating factor overall. Therefore, in order to increase future program uptake, we recommend focusing future educational efforts on fostering a sense of professional fulfillment among pharmacists; one method to accomplish this is to establish a system for regular feedback and support on program efforts.[297] Specifically, social gains were more motivating than social losses, economic gains were more motivating than economic losses, social legitimacy was more motivating than technical efficacy, and opportunity framing was more motivating than threat framing. We also found that economic gains and technical efficacy were negatively associated with intention to provide naloxone services at baseline, implying that economic factors are not effective elements to target in interventions aiming to enhance naloxone services implementation. Conversely, this implies that social factors may be better targets for interventions to enhance naloxone services. Overall, findings are partially consistent with Kennedy and Fiss' Motivations for Adopting Innovation model, which states that earlier adopters of an innovation are more motivated by both economic and social gains (versus losses), as well as opportunity framing (versus threat framing).[243] Specifically, social factors are the most motivating in this study. In light of these results, the training program in the current study can be improved by highlighting the social

gains associated with pharmacists offering naloxone services, such as professional fulfillment, helping patients, improving the local community, improving the image of their pharmacy, and being seen as a pharmacy leader.

5.3 Impact and Recommendations

Our results suggest that training programs created using a participatory design approach are an effective method to involve Alabama pharmacists in opioid overdose death prevention strategies in terms of increasing their confidence and intention to participate in naloxone services. This work will: 1) have a broad impact on patient care and public health; 2) improve pharmacy practice; and 3) add to the organizational adoption/implementation literature. The outcomes of this study are expected to inform adoption or adaptation of the training program in other states.

First, this study is expected to have a broad impact on patient care and public health. Given the high rate of opioid overdose deaths in the U.S. (over 10 per 100,000), especially in the southern and northeastern states, methods to prevent these deaths are sorely needed.[4,33,34] The state of Alabama is of particular concern, as it has the highest opioid prescribing rate in the country, but lacks a sufficient number of specialized opioid abuse treatment facilities and specially trained physicians.[7,8,35] Thus, by training community pharmacists to dispense naloxone to their full capacity, we will increase the number of providers who are capable of educating the public about opioid risks and providing services for patients using opioids, increase patient access to naloxone, and potentially prevent opioid overdose deaths.

Second, this study has the potential to improve pharmacy practice. Pharmacists have successfully adopted/implemented clinical care services such as immunizations and medication

therapy management (MTM).[36-46] However, their role in substance abuse treatment and overdose death prevention has been limited.[47] By creating a targeted training program to increase pharmacists' knowledge, confidence, and ability to dispense naloxone and overcome adoption/implementation barriers, we will advance the role of the pharmacist. This will potentially open up new practice areas for pharmacists and may increase pharmacy revenue streams and job satisfaction, thus improving not only patient care but also the profession of pharmacy.

Third, the results of this study will add to the organizational adoption/implementation literature. Currently, there is limited research regarding factors motivating community pharmacists' adoption or implementation of naloxone services.[48] Understanding of these factors will help to increase future program uptake and aid in adaptation of the program in other states. Furthermore, by assessing the impact of a targeted training program on implementation of naloxone services structure and process indicators, we gained further insight into strategies to overcome barriers and increase the extent of pharmacy-based naloxone services implementation at the organizational level.

However, we found that education is not enough to make a significant impact on naloxone services behaviors. Thus, strategies to further facilitate adoption of community pharmacy-based naloxone services are sorely needed. Opinion leaders, manager/owner change agents, and champions are feasible and relevant strategies that may be used to facilitate adoption of the program. Specifically, opinion leaders may be used to facilitate adoption of the program.[180,321] Opinion leaders may be pharmacists with well-connected interpersonal networks amongst other pharmacy staff, and whose opinions are respected due to past implementation of successful business practices.[180] Opinion leaders may facilitate adoption of naloxone services at

two stages in the adoption decision process: 1) knowledge; and 2) persuasion. First, opinion leaders may serve as internal change agents in roles as peer educators to increase community pharmacists' knowledge of naloxone services.[322] In fact, using immunization services as an example, peer academic detailing has been shown to increase provider pneumococcal vaccination rates by ten-fold.[323] Second, the Social Cognitive Theory supports the strategy of using opinion leaders, as it posits that modeling of a behavior by peers or respected individuals in one's social network leads to the desired behavior change;[313,324] in this case, modeling of naloxone services by opinion leaders in Alabama community pharmacies will lead to increased adoption of naloxone services in other pharmacies. Indeed, social network theory supports this model; as opinion leaders adopt naloxone services, peers linked via their interpersonal communication networks will be persuaded to adopt, leading to a "critical mass", at which point adoption of naloxone services will be self-sustaining.[180,325] Previous studies have shown success with this method, with opinion leaders used to improve physician use of evidence-based guidelines for patients with schizophrenia.[326]

Second, managers/owners may be used as change agents to facilitate adoption of the program. Community pharmacy managers/owners may serve as change agents in a top-down approach to increase community pharmacy staff members' knowledge about naloxone services and persuade them to adopt.[180] This strategy is supported by the Organizational Readiness for Change model, which states that organization members must be both willing and able to adopt an innovation.[180] Community pharmacy managers/owners can use internal channels of communication to increase pharmacy staff members' knowledge of naloxone services.[327] In line with Lewin's Three Step Model of the change process (unfreezing, moving, freezing), managers/owners can also provide evidence to pharmacy staff regarding the gap between their

current level of performance and the market or norm level in order to create an urgency in making changes and increase how much members value and are willing to adopt naloxone services.[327] Furthermore, managers/owners can provide a source of adoption persuasion by influencing the task demands, resources, and situational factors necessary for community pharmacy members to be able to adopt naloxone services.[180,328]

Third, champions may be used to facilitate adoption of the program. Champions may include community pharmacy opinion leaders or managers/owners, but may also be some other powerful or charismatic individual within the community pharmacy organization, including a technician or clerk.[180] The main role of the champion is to provide knowledge and persuade others to adopt naloxone services by acting as a "lobbyist."[180] This may be accomplished via methods to increase knowledge and skills like train-the-trainer,[329] which has shown benefits in cancer control settings.[330] Program champions may also serve to persuade members to adopt the program by reducing members' uncertainty regarding the innovation by emphasizing the fit or match between naloxone services and the pharmacy's values, size, and slack resources.[180] For example, if the pharmacy already implements patient counseling and MTM services, which are parallel to opioid counseling and naloxone services, then the champion can reduce uncertainty regarding naloxone services adoption by clearly emphasizing the fit between the pharmacy's current mission and the new program.[180] Indeed, using immunization services as an example again, use of respected colleagues or peers as program "champions" is shown to increase provider immunization rates by almost 20%,[331] increasing providers' willingness to participate in the program.[332] Furthermore, champions can be paired with additional strategies in order to facilitate the transition from intention to actual behavior change.[293,333] In particular, audit and

feedback as well as internal (within the change unit) plus external (outside the change unit) facilitation have been shown to be effective in bridging this intention-behavior gap.[334-336]

5.4 Limitations

There were several limitations to this study that must be mentioned. First, the sample size in Aim 1 was low (10 pharmacists). However, the purpose of these qualitative interviews was to gain a depth rather than a breadth of information, and saturation was reached. Next, the study was only conducted in the state of Alabama and may not be able to be generalized outside that state. Future studies can expand the scope of the EmpoweringCommunityPharrmacists training program to other states, and results could be compared to states with similar laws regarding naloxone provision. Furthermore, volunteer bias is of concern in Aims 1 and 2, whereby individuals who were most interested in the topic and motivated to make a change chose to participate.

In Aim 2, monthly contact with the study participants (email check-ins) as well as the Hawthorne effect may have had some impact on the behavior of the control group, motivating control group participants to learn about or participate in naloxone services to a greater extent than if they had not received reminders or if they had not known they were enrolled in a study. A carry-over effect, whereby participants were familiarized with knowledge questions and correct responses over repeated administration of the survey instrument, may have also resulted in increased knowledge scores within the control group over time. Additionally, the number of naloxone prescriptions dispensed was collected via self-report (Aim 2), which may introduce an element of recall bias. However, this method was chosen in order to minimize study burden on busy community pharmacists. Also, the study was conducted over 3 months, which may not be

enough to time to detect a sustained change in behaviors. However, this was the most feasible given the time constraints of the dissertation study. Lastly, we could not control for other training or education programs that may have been experienced by the participants during the course of this study. Considering the current national concern over opioid misuse, there are many other educational materials that participants could have been exposed to outside of the study. However, a randomized controlled trial design was used to minimize the effect of this type of history bias.

5.5 Future Directions and Conclusions

The EmpoweringCommunityPharmacists training program was effective at increasing pharmacists' intention and confidence to implement naloxone services. However, there was not enough evidence to conclude that the intervention had an effect on participants' knowledge about naloxone, attitudes towards naloxone services, perceived barriers to implementing naloxone services, number of structure activities completed, number of process activities engaged in, or number of naloxone prescriptions dispensed. The training program itself is crucial but not sufficient to affect behavior change. Therefore, additional implementation strategies should be used to facilitate and sustain the change transition in future studies.

Applying lessons learned from this study, the training program could be expanded to other counties in Alabama, or even other states with similar laws regarding naloxone provision. Furthermore, given ideal circumstances with unlimited time and resources to conduct the study, the follow-up period could be expanded to one to two years in order to assess sustained changes in knowledge, intention, beliefs, and behaviors. By offering multiple delivery formats, including live in-person, live webinar, and online home-study, we could also reach a wider audience. If

282

possible in the budget and time frame, we recommend incorporating a live workshop portion for naloxone administration, as this was preferred by interviewed pharmacists but was not feasible in the current study. However, we recommend no more than 3 hours total for the educational portion plus workshop, as this was the maximum time limit suggested by interviewed pharmacists. Internal and external facilitators, in addition to site champions, could serve to overcome barriers between intention and changes in naloxone services behavior post-training. We also recommend partnering with state and local professional organizations to help spread the word of the training program and assist with recruitment efforts. Involving these organizations would help to lend credibility to the program and disseminate it on a wider scale.

Furthermore, we can take the lessons learned from this study and expand the study to include other healthcare providers as well. Future studies may focus on interviewing both patients and prescribers in Alabama to explore their perceptions of pharmacy-based naloxone services, with the ultimate goal to create a patient-centered communication aid or tool to help pharmacists and prescribers communicate with patients about opioid overdose risk and naloxone. Not only can community healthcare providers be involved in naloxone services in this way, but a network of providers can also be created to help "close the loop," a key best practice or strategy recommended by experts in this study. There is a need to create a referral system or "opioid safety network" for patients with opioid use disorder between community pharmacies, prescribers, and treatment centers; however, little is known about the feasibility of such a system. Therefore, by partnering with local community healthcare providers, we will be able to create a stakeholder panel to explore this issue before creating, piloting, and scaling up such a network.

Future studies should test implementation strategies to increase naloxone uptake. The current study focused on education as one avenue to enhance naloxone services, but multiple

implementation strategies can be examined to assess their impact on the number of naloxone

prescriptions dispensed. One such strategy could be a system-oriented change, such as gaining

manager or corporate support, assigning staff roles, optimizing workflow, or adopting

technology to assist with naloxone provision (automated alerts within pharmacy dispensing

software, etc). Another strategy could focus on patients by creating demand via personal selling,

in-store advertisements, or media campaigns. In terms of focusing on patients, the impact of

various patient identification/communication strategies on naloxone uptake, especially the

targeted versus universal approach discussed in this study, could be investigated. By doing so,

we can discover the most effective strategies for enhancing naloxone services in community

pharmacies, helping us to target future educational efforts and translate our research findings into

practice. Ultimately, by enhancing community pharmacy-based naloxone services, we can then

potentially help to prevent opioid-related overdose deaths.

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Appendix A

Aim 1 Interview Protocol

Primary Questions: What does adoption/implementation of pharmacy-based naloxone services mean for pharmacists in Alabama?

Introduction: This interview is for the first phase of my dissertation study. It will help me to understand about Alabama community pharmacists' attitudes, experiences, and training needs regarding naloxone dispensing for opioid overdose prevention in the pharmacy setting. I'll use the results of the interview to help me create a naloxone training program targeted to Alabama community pharmacists' needs, which I will implement in the second phase of the project.

Warm-Up Questions:

1. How is your day going?
2. Can you tell me a bit about your experiences working in pharmacies / current practice site (where you have worked, for how long, etc)? **>> Setting of current pharmacy location.**
3. Can you tell me a bit about your background (professional history, etc)?

Domain 1: What are community pharmacists' / experts' experiences with opioid abuse/misuse in their professional roles?

1. What are your thoughts about the state of opioid abuse/misuse in…
   a. Alabama? **>> Tell me more about that.**
      i. If "nothing" **>> [Provide information] >> What do you think about that?**
   b. The country as a whole? **>> Tell me more about that.**

      i. If "nothing" **>> [Provide information] >> What do you think about that?**
2. Tell me a bit about your experiences regarding patient opioid abuse/misuse?
   a. Tell me about any specific situations or encounters that come to mind? **>> Tell me more about that.**

Domain 2: What are community pharmacists' / experts' experiences and opinions regarding pharmacy-based naloxone services?

1. What do you know about the laws in Alabama allowing pharmacists to dispense naloxone without a prescription? **>> Tell me more about that.**
   a. If "nothing" **>> [Provide information] >> What do you think about that?**
   b. What do you think about pharmacists being able to dispense naloxone to patients or caregivers using a state-wide standing order?
2. Community pharmacists: Tell me about a time you dispensed/administered naloxone to a patient (if ever)?
   a. If "yes" **>> Please walk me through that experience [may prompt to elaborate on the strategies used in the naloxone service]**
   b. What naloxone services are offered at your pharmacy? **>>Tell me more about that [may prompt about patient identification strategies, dosage forms stocked, communication with patients, etc].**
   [Keep implementation categories in mind: use evaluative and iterative strategies; provide interactive assistance; adapt and tailor to context; develop stakeholder interrelationships; train and educate stakeholders; support clinicians; engage consumers; utilize financial strategies; change infrastructure].

   Experts: Tell me a bit about your experiences regarding implementation of naloxone services? **>> [may prompt about teaching, treatment of patients, legal issues, setting up a naloxone service, research]**
3. Community pharmacists: When working in a community pharmacy, tell me what your thoughts would be about dispensing naloxone at your pharmacy? **>> Tell me more about that.**
   a. How do you think your staff would feel about dispensing naloxone?
   b. How do you think other pharmacists would feel about dispensing naloxone?

   Experts: Based on your experience, what best strategies would you recommend to community pharmacists regarding implementation of pharmacy-based naloxone services? **>> Tell me more about that [may prompt about identifying eligible patients, billing, stocking, workflow, resources].**
   [Keep implementation categories in mind: use evaluative and iterative strategies; provide interactive assistance; adapt and tailor to context; develop stakeholder interrelationships; train and educate stakeholders; support clinicians; engage consumers; utilize financial strategies; change infrastructure].

4. What things do you think would make it difficult for pharmacists to dispense naloxone without a prescription? **>> Tell me more about that [may prompt about billing, stocking, staff training].**
    a. How do you think these barriers can be overcome? **>> Tell me more about that**
       [Keep implementation categories in mind: use evaluative and iterative strategies; provide interactive assistance; adapt and tailor to context; develop stakeholder interrelationships; train and educate stakeholders; support clinicians; engage consumers; utilize financial strategies; change infrastructure].
5. Do you think pharmacist dispensing of naloxone will be well-received by patients? **>> Tell me more about that.**
    a. What would make patients more receptive to receiving naloxone from the pharmacy? **>>Tell me more about that.**
       [Keep implementation categories in mind: use evaluative and iterative strategies; provide interactive assistance; adapt and tailor to context; develop stakeholder interrelationships; train and educate stakeholders; support clinicians; engage consumers; utilize financial strategies; change infrastructure].
6. What are your thoughts about other practices (besides naloxone) that can be used to help prevent opioid overdose or abuse? **>> [May prompt about PDMP's, preventing over-prescribing, etc.]**

Domain 3: What are community pharmacists' needs and opinions regarding naloxone education/training?

1. What do you think pharmacists need the most training on in terms of **opioid addiction in general**? **>> Tell me more about that [may prompt about identifying red flags on prescriptions, who to contact about suspicious prescribing activity, naloxone, PDMP's, dispensing laws, etc]**
    a. Community pharmacists: What areas do you think that you yourself need more training in?
2. Do you think pharmacists are adequately trained to **dispense naloxone** without a prescription? **>> Tell me more about that.**
3. Community pharmacists: Do you feel that you yourself are adequately trained to **dispense naloxone** without a prescription?
4. What do you think are the most critical areas for pharmacist training in regards to dispensing naloxone without a physician's prescription? **>> [May prompt about billing, insurance, dispensing process, recipient of naloxone (patient or caregiver), how to identify at-risk patients, stocking, dosage forms of naloxone, counseling tips, mechanism of action of naloxone, documentation, etc].**

5. What do you think is the best format for pharmacist continuing education about naloxone? **>> [May prompt about online, webinar, paper-based, live, home-study, length of CE (hours), etc].**

Conclusion:

1. Thank you so much. That concludes all of my questions. Do you have any other questions or comments that you would like to make before we end?
2. I would also like to ask you to participate on a panel to help me create the naloxone training program. This would involve approximately 2 feedback sessions to help me modify and give input on the training (CE) program, once it is created later this year. May I contact you later about this?
3. Lastly, I will be sending you a link to a very brief (2-min) follow-up survey to get a bit more information about you and to allow you to make any comments that you might not have thought of during the interview. I will then send you a $20 gift card to thank you for your time for this interview.

Appendix B

Aim 1 Stakeholder Panel CE Feedback Questionnaire

Round 1 Feedback

Thank you for your help with my dissertation study, "Empowering community pharmacists to prevent opioid overdose deaths: development and implementation of a targeted naloxone training program." As I develop and finalize a training program focusing on practical strategies for Alabama community pharmacists to provide naloxone, your feedback is very important to me. Please briefly review Module 1, Module 2, and Module 3 of the training and use the questions below to comment on the accuracy, comprehensiveness, and flow of the content and format. This questionnaire should take no more than 10 minutes to complete.

Module 1: Naloxone Basics

Downloadable PowerPoint File: Module 1

On a scale of 1 to 5, with 1 being Strongly Disagree and 5 being Strongly Agree, please rate your level of agreement or disagreement with the following statements regarding Module 1.

	Strongly disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
I was satisfied with the information presented about the current opioid landscape	○	○	○	○	○
I was satisfied with the information presented about treatment and prevention of opioid use disorder	○	○	○	○	○
I was satisfied with the information presented about naloxone administration	○	○	○	○	○
I was satisfied with the information presented about naloxone dispensing laws in Alabama	○	○	○	○	○
I was satisfied with the information presented in Module 1 overall	○	○	○	○	○
The information presented in Module 1 was useful for practicing Alabama community pharmacists	○	○	○	○	○
The information presented in Module 1 was accurate	○	○	○	○	○

The information in Module 1 was presented in sufficient detail	○	○	○	○	○
The text in Module 1 was easy to read	○	○	○	○	○
The text in Module 1 loaded well on my device	○	○	○	○	○
The graphics in Module 1 loaded well on my device	○	○	○	○	○
The overall appearance of Module 1 was pleasing to the eye	○	○	○	○	○

What topics were not discussed in Module 1 that you wished were discussed?

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How can the content presented in Module 1 be improved? This may include the accuracy, depth, and usefulness of the information presented.

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How can the format of Module 1 be improved? Format may include such things as the flow, appearance, and readability.

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Module 2: Implementation Strategies

Downloadable PowerPoint File: Module 2

On a scale of 1 to 5, with 1 being Strongly Disagree and 5 being Strongly Agree, please rate your level of agreement or disagreement with the following statements regarding Module 2.

	Strongly disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
I was satisfied with the information presented about community pharmacists' role and scope	○	○	○	○	○
I was satisfied with the information presented about pharmacy-based naloxone service structures	○	○	○	○	○
I was satisfied with the information presented about pharmacy-based naloxone service processes	○	○	○	○	○
I was satisfied with the implementation resources provided in Module 2	○	○	○	○	○
I was satisfied with the information presented in Module 2 overall	○	○	○	○	○
The information presented in Module 2 was useful for practicing Alabama community pharmacists	○	○	○	○	○
The information presented in Module 2 was accurate	○	○	○	○	○

The information in Module 2 was presented in sufficient detail	○	○	○	○	○
The text in Module 2 was easy to read	○	○	○	○	○
The text in Module 2 loaded well on my device	○	○	○	○	○
The graphics in Module 2 loaded well on my device	○	○	○	○	○
The overall appearance of Module 2 was pleasing to the eye	○	○	○	○	○

What topics were not discussed in Module 2 that you wished were discussed?

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How can the content presented in Module 2 be improved? This may include the accuracy, depth, and usefulness of the information presented.

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How can the format of Module 2 be improved? Format may include such things as the flow, appearance, and readability.

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Module 3: Communication Strategies

Downloadable PowerPoint File: Module 3

On a scale of 1 to 5, with 1 being Strongly Disagree and 5 being Strongly Agree, please rate your level of agreement or disagreement with the following statements regarding Module 3.

	Strongly disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
I was satisfied with the information presented about types of communication approaches	○	○	○	○	○
I was satisfied with the information presented about creating a culture of safety	○	○	○	○	○
I was satisfied with the information presented about using elements of motivational interviewing (MI)	○	○	○	○	○
I was satisfied with the language used in communication examples	○	○	○	○	○
I was satisfied with the information presented in Module 3 overall	○	○	○	○	○
The information presented in Module 3 was useful for practicing Alabama community pharmacists	○	○	○	○	○
The information presented in Module 3 was accurate	○	○	○	○	○

The information in Module 3 was presented in sufficient detail	○	○	○	○	○
The text in Module 3 was easy to read	○	○	○	○	○
The text in Module 3 loaded well on my device	○	○	○	○	○
The graphics in Module 3 loaded well on my device	○	○	○	○	○
The overall appearance of Module 3 was pleasing to the eye	○	○	○	○	○

What topics were not discussed in Module 3 that you wished were discussed?

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How can the content presented in Module 3 be improved? This may include the accuracy, depth, and usefulness of the information presented.

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How can the format of Module 3 be improved? Format may include such things as the flow, appearance, and readability.

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Overall

What additional topics should be discussed that were not already presented in Modules 1-3?

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What other comments do you have regarding the training program's content and format that you have not yet had a chance to mention?

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Appendix C

Aim 2 General Information Flyer

TECHNICIAN: Use product information on card to fill and process insurance or provide cash price to patient. Get pharmacist for verification and counseling.

PHARMACIST: Counsel patient on overdose prevention and the steps of overdose response: *check for response, call 911, give naloxone, rescue breathe or give chest compressions, stay with patient*

SUSPECT OVERDOSE?
1. Check for response
2. Call 911
3. Give naloxone. If no response in 2-3 minutes, repeat dose.
4. Give rescue breaths or chest compressions.
5. Stay with person until help arrives

A

MULTI-STEP NASAL SPRAY

DIRECTIONS: Spray 1 mL (half of the syringe) into each nostril.

QUANTITY: #2 x2 mL Luer-Jet™ Luer-Lock needleless syringe plus #2 mucosal atomizer devices (MAD-300)

SIG: Spray 1 mL (1/2 of syringe) into each nostril.

NDC: 76329-3369-01

COST: $-$$

B

SINGLE-STEP NASAL SPRAY

DIRECTIONS: Spray full dose into one nostril.

QUANTITY: #1 two-pack of two 4mg/0.1 mL intranasal devices)

SIG: Spray .1 mL into one nostril.

NDC: 69547-353-02

COST: $$$

C

INTRAMUSCULAR INJECTION

DIRECTIONS: Inject 1 mL in shoulder or thigh.

QUANTITY: #2 single-use 1 mL vials PLUS #2 3 mL syringe w/ 23-25 gauge 1-1.5 inch IM needles

SIG: Inject 1 mL in shoulder or thigh.

NDC: 00409-1215-01
67457-0292-02

COST: $-$$

D

AUTO-INJECTOR

DIRECTIONS: Use as directed by voice-prompt. Press black side firmly on outer thigh.

QUANTITY: #1 two-pack of two 0.4 mg/0.4 mL prefilled auto-injector devices

SIG: Inject into outer thigh as directed by English voice-prompt system. Place black side firmly on outer thigh and depress and hold for 5 seconds.

NDC: 60842-030-01

COST: $$$$*

*Coupons available, see evzio.com for more info

FOR ALL PRODUCTS, repeat naloxone administration after 2–3 minutes if there is no response.

Naloxone is a medicine that can stop an overdose from pain medication, methadone, or heroin.

People at risk for overdose and their family and friends should know how to avoid overdose. Learn how to spot overdose and how to respond to save a life.

For more on opioid safety, videos on how to use naloxone, or to get help for addiction, go to PrescribetoPrevent.org

PRESCRIBE TO PREVENT

BOSTON MEDICAL CENTER

Publicly available at PrescribetoPrevent.org

STANDING ORDER OF THE STATE HEALTH OFFICER
NALOXONE DISTRIBUTION FOR OVERDOSE PREVENTION

Naloxone Hydrochloride (naloxone) is an opioid antagonist indicated for the reversal of an opioid overdose, whether from legally prescribed opioids or from illegal opioids such as heroin or illegally produced fentanyl, in the setting of respiratory depression or unresponsiveness. It may be delivered intranasally with a mucosal atomizer device, intranasally with a nasal spray, or intramuscularly with a needle.

I.   PURPOSE

This standing order is intended to ensure that naloxone is readily obtainable by any person who is:

  A. An individual at risk of experiencing an opioid-related overdose; or
  B. A family member, friend, or other individual, including law enforcement, fire department, rescue squad, and volunteer fire department personnel, who is in a position to assist a person at risk of experiencing an opioid-related overdose.

II. AUTHORITY

This standing order is issued pursuant to Act 2016-307, which authorizes the State Health Officer to prescribe naloxone via standing order.

III. AUTHORIZATION

This standing order may be used as a prescription to obtain naloxone from a pharmacy in the event there is an inability to obtain naloxone or a prescription for naloxone from an eligible person's regular health care provider or another source. This order is authorization for pharmacists to dispense naloxone and devices for its administration solely in the forms prescribed herein.

IV. ORDER TO DISPENSE

Upon receipt of written communication that provides a factual basis for a reasonable conclusion that the person to receive the naloxone is an eligible person, **and** upon receipt of basic instruction and information on how to recognize and respond to a possible opioid overdose and how to administer naloxone, dispense one naloxone kit. (*Refer further to Protocol, Pharmacist Actions set out on page 5.*) Naloxone kits may be dispensed in bulk quantities to law enforcement agencies, fire departments, rescue squads, and volunteer fire departments. Pharmacists should use clinical judgment to determine preferred formulation. Unlimited refills are authorized.

  A. Intranasal naloxone with atomizer kits must contain a minimum of the following:

      -   Two 2-mL Luer-Jet Luer-lock syringes prefilled with naloxone hydrochloride
      -   Two mucosal atomization devices (MAD).

- Step-by-step instructions for administration of intranasal naloxone including a possible second dose, along with basic instructions on calling 911, providing rescue breathing, and monitoring the overdose victim until professional help arrives.

B. Intranasal naloxone spray kits must contain a minimum of the following:

- One package of two doses of naloxone nasal spray.
- Step-by-step instructions for administration of intranasal naloxone including a possible second dose, along with basic instructions on calling 911, providing rescue breathing, and monitoring the overdose victim until professional help arrives.

C. Intramuscular naloxone kits must contain a minimum of the following:

- Two single-use 1mL vials of naloxone hydrochloride.
- Two intramuscular needles with syringes.
- Step-by-step instructions for administration of intramuscular naloxone including a possible second dose, along with basic instructions on calling 911, providing rescue breathing, and monitoring the overdose victim until professional help arrives.

D. Intramuscular auto-injector naloxone kits must contain a minimum of the following:

- One naloxone hydrochloride prepackaged kit containing two auto-injectors with audio instructions and one training device.
- Step-by-step instructions for administration of intramuscular naloxone including a possible second dose, along with basic instructions on calling 911, providing rescue breathing, and monitoring the overdose victim until professional help arrives.

V. APPROPRIATE USE AND DIRECTIONS

A. Call 911 as soon as possible for a person suspected of an overdose with respiratory depression or unresponsiveness and initiate rescue breathing.

B. Administer naloxone as follows (pharmacist to indicate to the client which instructions to follow based upon the form of naloxone being dispensed):

1. Intranasal naloxone with syringe and atomizer:

- Pop off two colored caps from the delivery syringe and one from the naloxone vial.
- Screw the naloxone vial gently into the delivery syringe.
- Screw the mucosal atomizer device onto the tip of the syringe.
- Spray half (1mL) of the naloxone in one nostril and the other half (1mL) in the other nostril.
- Repeat if there is no response after 3 minutes, or if the victim relapses back into respiratory depression or unresponsiveness before emergency assistance arrives.

2. Intranasal naloxone with Narcan® Nasal Spray:

- Deliver one spray into one nostril. (Do not "prime" or test the spray device before spraying it into the nostril, as this will waste the medicine.)
- Repeat with the second nasal spray device in the opposite nostril if there is no response after 2-3 minutes, or if the victim relapses back into respiratory depression or unresponsiveness before emergency assistance arrives.

3. Intramuscular naloxone with syringe and needle:

- Uncap the naloxone vial and uncap the needle on the syringe.
- Insert the needle through the rubber membrane on the naloxone vial, turn the vial upside down, draw up 1mL of naloxone liquid, and withdraw the needle.
- Insert the needle into the muscle of the upper arm or thigh of the victim, through the clothing if needed, and push the plunger to inject all of the naloxone.
- Repeat the injection with second 1mL vial of naloxone if there is no response after 3 minutes, or if the victim relapses back into respiratory depression or unresponsiveness before emergency assistance arrives.

4. Intramuscular naloxone with Evzio® Auto-injector:

- Pull auto-injector from outer case.
- Pull off red safety guard.
- Place the black end of the auto-injector against the outer thigh, through clothing if needed, press firmly and hold in place for 5 seconds.
- Repeat with the second auto-injector if no response after 3 minutes, or if the victim relapses back into respiratory depression or unresponsiveness before emergency assistance arrives.

C. Continue to monitor respiration and responsiveness of the victim, and continue to provide rescue breathing as necessary until emergency assistance arrives.

VI. CONTRAINDICATIONS

Do not administer naloxone to a person with known hypersensitivity to naloxone or to any of the other ingredients listed in the packaging insert for naloxone.

VII. PRECAUTIONS

Respiratory depression due to other drugs. Naloxone is not effective against respiratory depression due to non-opioid drugs. Initiate rescue breathing or CPR as indicated and call 911.

VIII. ADVERSE REACTIONS

Opioid depression. Abrupt reversal of opioid depression may result in nausea, vomiting, sweating, abnormal heart beats, fluid development in the lungs, opioid acute withdrawal syndrome, increased blood pressure, shaking, shivering, seizures, and hot flashes.

IX. EXPIRATION AND REVIEW

This standing order will automatically expire on the date naloxone may be approved as an over-the-counter medication. This standing order will be reviewed, and may be updated, if there is relevant new science about naloxone administration and will be posted at http://www.alabamapublichealth.gov, search naloxone.

_____   _____
Scott Harris, M.D., M.P.H.   3/8/18
State Health Officer   Date
NPI Number: 1992713408
License Number: MD.16614

PROTOCOL FOR NALOXONE STANDING ORDER

I. Indications and Usage

Naloxone is indicated for the complete or partial reversal of opioid overdose induced by natural or synthetic opioids, and evidenced by respiratory depression or unresponsiveness.

II. Assessment

- There is a factual basis for a reasonable conclusion that the individual to receive the naloxone is an individual at risk of experiencing an opioid-related overdose, or is a family member, friend, or other individual in a position to assist an individual at risk of experiencing an opioid-related overdose.
- The individual to whom the naloxone is dispensed is able to understand the essential components of overdose recognition and response and naloxone administration.
- The person to potentially be administered naloxone, if known, does not have a history of known serious adverse reaction to naloxone. Note that opioid withdrawal symptoms, including body aches, abdominal cramps, diarrhea, nausea or vomiting, increased heart rate, restlessness or irritability, shivering or trembling, can be expected with reversal of an opioid overdose, and should not be equated with a serious adverse reaction to naloxone.

III. Pharmacist Actions

- Provide basic instruction on recognition of opioid overdose, calling 911, rescue breathing, and administration of naloxone as described in the Standing Order.
- Dispense naloxone kit and explain contents to the individual.
- Counseling: Offer information on risk factors for opioid overdose, overdose prevention measures, risk and recognition of addiction, and resources for mental health and addiction treatment services.
- Have client complete and sign Client Form (page 6) attesting to need for naloxone, receipt of instructions, and offer of counseling. If bulk dispensing to a law enforcement agency, fire department, rescue squad, or volunteer fire department, have the agency representative complete and sign the Agency Form (page 7).
- Keep a record of all clients who have received naloxone via this standing order.

_____   ___3/8/18___
Scott Harris, M.D., M.P.H.   Date
State Health Officer
NPI Number: 1992713408
License Number: MD.16614

Naloxone Client Form

1. Check one:

a) ___ I am an individual at risk of experiencing an opioid-related overdose.

b) ___ I am a family member, friend, or other individual in a position to assist an individual at risk of experiencing an opioid-related overdose.

Write in this box the facts that support the statement checked above (this information will be kept confidential, but it is needed to verify your need for naloxone):

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2. ___ I have received information on how to recognize and respond to a possible opioid overdose.

3. ___ I have received basic instructions on how to administer naloxone.

4. ___ I have been offered information/counseling on risk factors for opioid overdose, overdose prevention measures, risk and recognition of addiction, and resources for mental health and addiction treatment services.

I understand that I may administer naloxone to another individual if I have a good faith belief that the individual is experiencing an opioid-related overdose, and if I exercise reasonable care in administering the naloxone.

Signature: _____   Date Signed: _____

Print Name: _____   Date of Birth: _____

Naloxone Agency Form

I am a representative of an agency that responds to emergencies involving individuals who may be at risk of experiencing an opioid-related overdose or to emergencies that may place the first responder at risk for exposure to opioids.

Name of Agency: _____

Write in this box the facts that support the statement checked above (this information will be kept confidential, but it is needed to verify your need for naloxone):

```
+---------------------------------------------------------------+
|                                                               |
|                                                               |
|                                                               |
|                                                               |
|                                                               |
|                                                               |
|                                                               |
+---------------------------------------------------------------+
```

I have received information on how to recognize and respond to a possible opioid overdose.

I have received basic instructions on how to administer naloxone.

I will ensure that all persons within my agency who have access or who may at some time administer naloxone are trained.

Signature: _____   Date Signed: _____

Print Name: _____   Date of Birth: _____

fax

TO: _____   FROM: _____

FAX: _____   PAGES: _____

PHONE: _____   DATE: _____

RE: _____   CC: _____

☐ [Urgent]   ☐ [For Review]   ☐ [Please Comment]   ☐ [Please Reply]   ☐ [Please Recycle]

Comments:

Patient Name: _____   DOB: _____

Dear Dr.

Today we dispensed naloxone to your patient as a safety precaution. We discussed signs of opioid overdose and reviewed how to administer naloxone in case of an emergency. Below is a summary of what we dispensed for your records:

	Name	Directions for Use	Quantity	Refills
Form of Naloxone Dispensed				
☐	Narcan nasal spray 4mg	Administer as directed prn for suspected overdose	1 (2-pack)	2
☐	Evzio auto-injector 2mg	Administer as directed prn for suspected overdose	1 (2-pack)	2
☐	Naloxone 0.4 mg/mL vial with 23/25G 1" syringe	Administer as directed prn for suspected overdose	2	2
☐	Naloxone 1 mg/mL PFS with 23/25G 1" needle or mucosal atomizing device (MAD)	Administer as directed prn for suspected overdose	2	2

Thank you.

Pharmacist: _____

Empowering
Community
Pharmacists.org

Naloxone for Patients

You or a loved one may be at risk for an accidental drug overdose.

Drug overdose is the leading cause of injury death in the United States. Most overdoses involve opioids, which include certain prescription pain relievers and heroin.

Common Opioids	Morphine (MS Contin®), Oxycodone (OxyContin®/Percocet®), Hydromorphone (Dilaudid®), Oxymorphone (Opana®), Fentanyl (Duragesic®), Hydrocodone (Vicodin®/Norco®), Codeine, Methadone, Heroin

Thousands of people die each year from accidental overdoses related to prescription drugs they were taking as directed. The pharmacist has determined you or a loved one may be at risk for an accidental opioid overdose for one or more of the following reasons:

✔	**Risk Factors for Opioid Overdose**
	History of opioid poisoning or overdose
	History of illicit or nonmedical opioid use
	Use of methadone or buprenorphine for opioid use disorder
	High-dose prescription opioid use (>50 milligram morphine equivalents daily)
	Long-term prescription opioid use (>90 days continuously for non-cancer pain)
	Long-acting or extended-release prescription opioid use
	Use of opioids from multiple prescribers or multiple pharmacies
	Use of interacting drugs or medications (alcohol, sedatives, antidepressants)
	Underlying disease of key organs (lung, kidney, liver, heart, HIV/AIDS)
	Recent release from drug treatment/detoxification or correctional facility

You should have naloxone at home to keep you and your loved ones safe.

Naloxone is the antidote to an opioid overdose. If you take too much of an opioid medication, your brain will stop telling your lungs to breathe. If this occurs, taking naloxone can save your life by allowing you to breathe again. Naloxone is not a controlled substance and it cannot be abused.

If you give naloxone to someone who is not experiencing an opioid overdose, nothing will happen. The only serious side-effect of naloxone is that it can cause withdrawal symptoms if the overdose victim has developed a physical dependence to opioids. While acute opioid withdrawal is not generally life-threatening, it is still essential to call emergency medical services. If you try to save someone's life with naloxone, you are protected by law from any liability regardless of the outcome.

Naloxone is available in several different versions. Some versions of naloxone are injected into the victim's muscle, while others can be squirted into their nose. Your pharmacist can help you determine which version of naloxone is right for you based on cost and ease-of-use. Check out **OperationNaloxone.org** to learn more about staying safe with opioids.

OPERATION NALOXONE.org

THINGS YOU MAY NOT KNOW
ABOUT ACCIDENTAL OPIOID OVERDOSE

238M PRESCRIPTIONS
for opioid medications were filled in 2011, up from 82M in 2001[1]

R_X opioids

DEATH RATE ▼

Deaths per 100,000 people

20
15
10
5
0

2000   2005   2010

Year
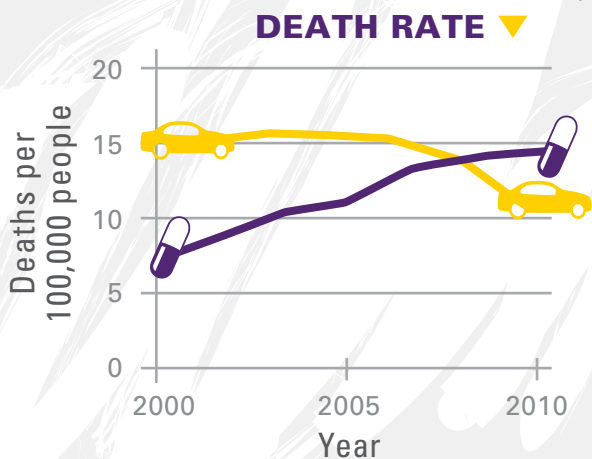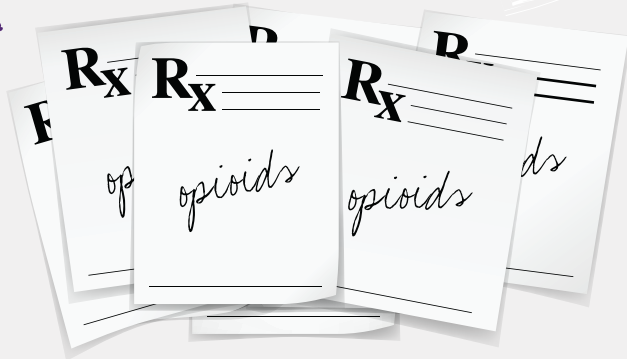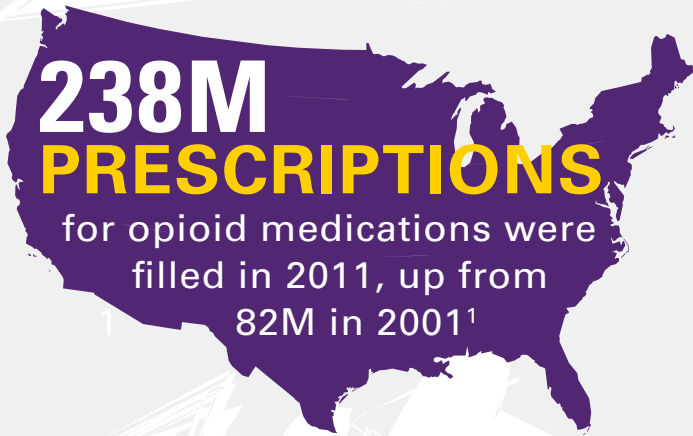
DRUG POISONING has now surpassed **AUTOMOBILE COLLISIONS** as the leading cause of accidental death in the US, driven largely by prescription opioids[2]

In 2010, there were

16,651 DEATHS CAUSED BY OPIOID OVERDOSE,
more than 13,000 of which were unintentional[3]

THAT'S ONE PERSON
36:00
EVERY 36 MINUTES[4]

UP TO 60% OF OPIOID OVERDOSE DEATHS
occur in medical users[4]

330

475,000
EMERGENCY DEPARTMENT VISITS
in 2009 were due to the misuse and abuse of prescription opioids[5]

500K

250K

0

2004   **2009**
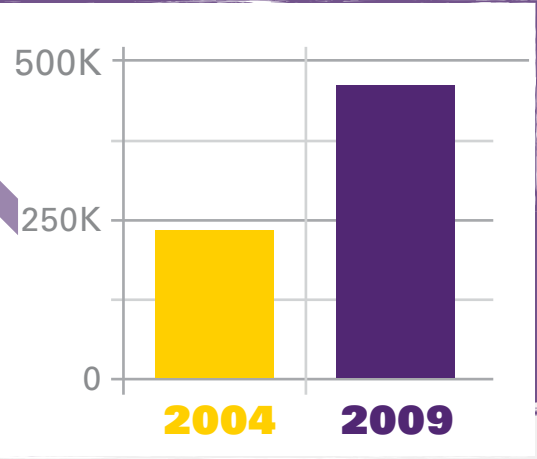
Opioid medications have a relatively narrow therapeutic window, meaning that even small changes
– such as a single extra dose or the addition of a small amount of alcohol –

CAN CAUSE A POTENTIALLY FATAL OVERDOSE[6]

Some risk factors include[7]:

High dosage of opioids

Taking certain medications in combination with an opioid

Having history of respiratory conditions
(such as asthma, COPD or sleep apnea)

In the event of an opioid overdose, seek emergency medical attention

Some signs include[8]:

✓ Very slow or absent breathing

✓ Loss of consciousness

✓ Extremely small pupils

1. Manchikanti L, Helm S 2nd, Fellows B, et al. Opioid epidemic in the United States. *Pain Physician.* 2012;15(3 Suppl):ES9–ES38.
2. National Center for Health Statistics. NCHS data on drug poisoning deaths. http://cdc.gov/nchs/data/factsheets/factsheet_drug_poisoning.pdf. Accessed May 16, 2014.
3. Centers for Disease Control and Prevention. Opioid-related deaths continue to increase. http://media.jsonline.com/images/OPIOIDS20GFIX.jpg. Accessed May 16, 2014.
4. Centers for Disease Control and Prevention.CDC grand rounds: prescription drug overdoses—a U.S. epidemic. *MMWR Morb Mortal Wkly Rep.* 2012;61:10–13.
5. Centers for Disease Control and Prevention. Policy Impact: Prescription Painkiller Overdose. November 2011.
6. Boyer EW. Management of opioid analgesic overdose. *N Engl J Med.* 2012;367(2):146–155.
7. Leavitt, SB. Intranasal naloxone for at-home opioid rescue. *Pract Pain Manag.* www.practicalpainmanagement.com/treatments/pharmacological/opioids/intranasal-naloxone-home-opioid-rescue. Accessed May 16, 2014.
8. Substance Abuse and Mental Health Services Administration. Opioid overdose toolkit: information for prescribers. http://store.samhsa.gov/product/Opioid-Overdose Prevention-Toolkit/SMA13–4742. Accessed May 16, 2014.

DO YOU OR SOMEONE YOU KNOW TAKE OPIOIDS?

NALOXONE (NARCAN) RESCUE KITS ARE AVAILABLE

Opioids include hydrocodone, oxycodone, codeine, hydromorphone, morphine, fentanyl, buprenorphine, methadone, oxymorphone, and heroin.

Someone who has overdosed will be unresponsive, have trouble breathing, and can die without immediate help.

If someone overdoses, call for help and use Narcan.

SAVE A LIFE.

332

Baseline Survey

Empowering Community Pharmacists to Prevent Opioid Overdose Deaths by Dispensing Naloxone: A Dissertation Study

Thank you for your participation in this dissertation study! This is the 1st of 3 surveys to help us better understand Alabama community pharmacists' knowledge, attitudes, confidence, and barriers in providing naloxone services. Although we will ask about your current naloxone practices and activities, you do not need to dispense naloxone in order to participate in this study. This survey has 7 parts and should take approximately 15 minutes to complete.

As a reminder, the informed consent document explaining the details of the study can be reviewed HERE. By continuing, you agree to participate in the study as described. Your participation can be withdrawn at any time.

Please complete this survey by December 5th, 2018. Thank you!

PART 1
KNOWLEDGE ABOUT NALOXONE (O1,O2, O3)

Please answer the following questions about naloxone to the best of your ability. This will help us to understand future areas for training and how we can help.

1. How long does naloxone take to have an effect?

   ○ 2-5 minutes

   ○ 6-10 minutes

   ○ 11-20 minutes

   ○ 21-40 minutes

2. Where is the most recommended place for non-experts to administer naloxone?

   ○ A. Outside of thigh / upper arm (intramuscular injection)

   ○ B. Any vein (intravenous injection)

   ○ C. By mouth

   ○ D. Intranasally

   ○ E. Both A and D

3. For how long do the effects of naloxone last?

    ◯ Less than 20 minutes

    ◯ About an hour

    ◯ 1-6 hours

    ◯ 6-12 hours

---

4. If the first dose of naloxone has no effect, a second dose can be given.

    ◯ True

    ◯ False

---

5. The effect of naloxone is shorter than the effect of heroin or methadone.

    ◯ True

    ◯ False

---

6. Under Alabama law, pharmacists are protected from civil and criminal liability for providing naloxone.

    ◯ True

    ◯ False

---

7. Commercially available forms of naloxone for outpatient pharmacy dispensing include which of the following? Please check all that apply.

    ☐ Auto-injector

    ☐ Nasal spray

    ☐ Injection vial + intramuscular (IM) syringe

    ☐ Prefilled syringe +/- mucosal atomizer

PART 2
CURRENT NALOXONE SERVICES (O1, O2, O3)

---

1. Do you currently offer naloxone services at your pharmacy? Naloxone services are defined as any system by which your pharmacy provides naloxone to at-risk patients, their caregivers, or first responders.

    ◯ Yes ➡ Continue to Part 2, Question 2

    ◯ No ➡ Skip to Part 2, Question 4

---

2. What methods do you use to provide naloxone to customers at your pharmacy? Check all that apply.

☐ Fill naloxone prescriptions written by physicians that are sent or brought in to the pharmacy

☐ Ask patient / caregiver to obtain a prescription from their physician

☐ Contact a physician to prescribe naloxone for the patient / caregiver

☐ Provide using Alabama's statewide standing order

☐ Provide using a collaborative practice agreement with a physician

☐ Other. Please specify: _____

---

3. To which type(s) of patients do you offer/provide naloxone? Check all that apply.

☐ Individuals prescribed high-dose opioids, other high-risk medications, or with a medical condition putting them at increased risk of overdose

☐ Any individual who is prescribed an opioid medication, regardless of perceived overdose risk

☐ Individuals with a history of illicit opioid use

---

4. On a scale of 1 to 7, please rate the extent to which you agree or disagree with the following statements regarding your **INTENTIONS** to offer/continue offering naloxone services at your pharmacy, with 1 being strongly disagree and 7 being strongly agree.

In the next 3 months, I intend to:

	Strongly disagree (1)	Disagree	Somewhat disagree	Neither agree nor disagree	Somewhat agree	Agree	Strongly agree (7)
Proactively identify patients who would benefit from naloxone	○	○	○	○	○	○	○
Initiate a conversation with a patient regarding the need for take-home naloxone	○	○	○	○	○	○	○
Stock naloxone products in my pharmacy	○	○	○	○	○	○	○
Dispense naloxone if prescribed by a physician	○	○	○	○	○	○	○
Dispense naloxone using Alabama's statewide standing order, if indicated	○	○	○	○	○	○	○

PART 3
ATTITUDES AND CONFIDENCE IN PROVIDING NALOXONE SERVICES (O1, O2, O3)

1. On a scale of 1 to 7, please rate the extent to which you agree or disagree with the following statements regarding your **ATTITUDES** toward pharmacy-based naloxone services, with 1 being strongly disagree and 7 strongly agree.

I believe that:

	Strongly disagree	Disagree	Somewhat disagree	Neither agree nor disagree	Somewhat agree	Agree	Strongly agree
Supplying naloxone in pharmacies encourages inappropriate use of opioids	○	○	○	○	○	○	○
It is unethical to supply naloxone to people who use opioids	○	○	○	○	○	○	○
It is part of a pharmacists' professional duty to provide naloxone to people who use opioids	○	○	○	○	○	○	○
People who inject illicit opioid drugs visiting my pharmacy would have a damaging effect on business	○	○	○	○	○	○	○
People who take high-dose opioid prescriptions visiting my pharmacy would have a damaging effect on business	○	○	○	○	○	○	○
It is appropriate for pharmacists to provide naloxone to people who inject illicit opioids	○	○	○	○	○	○	○
It is appropriate for pharmacists to provide naloxone to people who use prescription opioids	○	○	○	○	○	○	○
It is appropriate for pharmacists to contact physicians to obtain a naloxone prescription for eligible patients	○	○	○	○	○	○	○
Supplying naloxone at the pharmacy will help reduce opioid overdose deaths	○	○	○	○	○	○	○
I have no sympathy for people who misuse opioids	○	○	○	○	○	○	○
Offering naloxone in pharmacies is a good use of time and money	○	○	○	○	○	○	○
Pharmacists have a role to play in opioid overdose prevention	○	○	○	○	○	○	○
Other pharmacists will support my decision to supply naloxone in my	○	○	○	○	○	○	○

336

pharmacy

I feel comfortable supplying naloxone to people who inject illicit opioids

○ ○ ○ ○ ○ ○ ○

I feel comfortable supplying naloxone to people who take high-dose opioid prescriptions

○ ○ ○ ○ ○ ○ ○

---

2. On a scale of 1 to 7, please rate the extent to which you agree or disagree with the following statements regarding your **CONFIDENCE** in performing naloxone-related activities in your pharmacy, with 1 being strongly disagree and 7 being strongly agree.

I am confident in my ability to:

	Strongly disagree	Disagree	Somewhat disagree	Neither agree nor disagree	Somewhat agree	Agree	Strongly agree
Proactively identify patients who would benefit from naloxone	○	○	○	○	○	○	○
Communicate with physicians or other providers regarding their patients who may benefit from naloxone	○	○	○	○	○	○	○
Initiate a conversation with a patient regarding the need for take-home naloxone	○	○	○	○	○	○	○
Educate patients to recognize opioid overdose	○	○	○	○	○	○	○
Counsel patients on how to safely administer naloxone when indicated	○	○	○	○	○	○	○
Discuss naloxone cost with patients	○	○	○	○	○	○	○
Stock naloxone products in my pharmacy	○	○	○	○	○	○	○
Dispense naloxone products in my pharmacy when prescribed by a physician	○	○	○	○	○	○	○
Dispense naloxone products in my pharmacy using Alabama's statewide standing order	○	○	○	○	○	○	○
Correctly bill insurance companies for dispensed naloxone products	○	○	○	○	○	○	○

PART 4
BARRIERS TO PROVIDING PHARMACY-BASED NALOXONE SERVICES (O1, O2, O3)

1. On a scale of 1 to 7, please rate the extent to which you agree or disagree with the following statements regarding **BARRIERS** to providing naloxone services in your pharmacy, with 1 being strongly disagree and 7 being strongly agree.

Factors that make it difficult to provide naloxone services:

	Strongly disagree	Disagree	Somewhat disagree	Neither agree nor disagree	Somewhat agree	Agree	Strongly agree
The level of general support from management, corporate, or owners is low	◯	◯	◯	◯	◯	◯	◯
The level of general support from other pharmacists for naloxone services is low	◯	◯	◯	◯	◯	◯	◯
The level of general support from technicians for naloxone services is low	◯	◯	◯	◯	◯	◯	◯
The level of general support from local physicians is low	◯	◯	◯	◯	◯	◯	◯
I am unfamiliar with my state's laws and regulations about naloxone	◯	◯	◯	◯	◯	◯	◯
Pharmacy technician staff are not sufficiently trained to implement naloxone services	◯	◯	◯	◯	◯	◯	◯
It is difficult to package or stock the various forms of naloxone	◯	◯	◯	◯	◯	◯	◯
Naloxone expiration dates are too short	◯	◯	◯	◯	◯	◯	◯
The cost of stocking naloxone is too high	◯	◯	◯	◯	◯	◯	◯
It is difficult to obtain reimbursement from third-party payers	◯	◯	◯	◯	◯	◯	◯
The amount patients have to pay for naloxone is too high	◯	◯	◯	◯	◯	◯	◯
There is not enough profit margin	◯	◯	◯	◯	◯	◯	◯
Dispensing naloxone is too time-consuming	◯	◯	◯	◯	◯	◯	◯

Counseling patients about naloxone is too time-consuming	○	○	○	○	○	○	○
There are not enough pharmacy staff members	○	○	○	○	○	○	○
It is difficult to identify patients who would benefit from naloxone	○	○	○	○	○	○	○
Patients are not interested in receiving naloxone from the pharmacy	○	○	○	○	○	○	○
There are concerns over clientele who might frequent the pharmacy if naloxone services were in place	○	○	○	○	○	○	○
There are moral or ethical concerns associated with increasing drug abuse as a result of providing naloxone	○	○	○	○	○	○	○
There is community opposition to providing naloxone	○	○	○	○	○	○	○

PART 5
DEVELOPING & IMPLEMENTING NALOXONE SERVICES (O1, O3)

---

1. On a scale of 1 to 7, please rate your **PROGRESS** in completing the following naloxone service development activities at your pharmacy in the past 3 months, with 1 being no progress and 7 being completed. These are activities needed to build a naloxone service at your pharmacy.

In the past 3 months, I or my pharmacy staff:

	No Progress or Not Started	Minimal Progress	Some Progress	A Fair Amount of Progress	A Lot of Progress	Almost Completed	Completed
Prepared an action plan for offering naloxone services	○	○	○	○	○	○	○
Established staff member roles for naloxone services	○	○	○	○	○	○	○
Selected a person who is in charge of naloxone services	○	○	○	○	○	○	○
Approached management, corporate, or owners to gain support	○	○	○	○	○	○	○
Prepared an outreach/marketing plan for naloxone	○	○	○	○	○	○	○
Decided which naloxone products to stock	○	○	○	○	○	○	○

Established naloxone stocking procedures	○	○	○	○	○	○	○
Set a goal or objective for naloxone services	○	○	○	○	○	○	○
Adjusted prescription dispensing workflow to allow for greater naloxone services activity	○	○	○	○	○	○	○
Arranged staff schedules to accommodate naloxone services	○	○	○	○	○	○	○
Established a procedure to identify patients who would benefit from naloxone	○	○	○	○	○	○	○
Established a procedure to document naloxone dispensing	○	○	○	○	○	○	○
Established a procedure to follow-up with patients if naloxone was not in stock	○	○	○	○	○	○	○
Developed the budget for naloxone services	○	○	○	○	○	○	○
Established a plan to continuously evaluate and improve the pharmacy's naloxone services	○	○	○	○	○	○	○
Established access to my state's Prescription Drug Monitoring Program (PDMP)	○	○	○	○	○	○	○

2. On a scale of 1 to 7, please rate **HOW OFTEN YOU ENGAGED** in the following naloxone service activities at your pharmacy in the past 3 months, with 1 being never and 7 being very frequently. These are activities you may perform as part of a pharmacy-based naloxone service.

In the past 3 months, I or my pharmacy staff:

	Never	Very Infrequently	Infrequently	Sometimes	Fairly Often	Frequently	Very Frequently
Conducted staff meetings to discuss plans for naloxone services	○	○	○	○	○	○	○
Identified patients who could benefit from naloxone based on medication profile	○	○	○	○	○	○	○
Identified patients who could benefit from naloxone based on medical history screening	○	○	○	○	○	○	○

Identified patients who could benefit from naloxone based on non-prescription consultations	○	○	○	○	○	○	○
Stocked / continued stocking at least one naloxone dosage form	○	○	○	○	○	○	○
Educated patient(s) or caregiver(s) on how to recognize an opioid overdose	○	○	○	○	○	○	○
Counseled patient(s) or caregiver(s) on how to correctly administer naloxone	○	○	○	○	○	○	○
Provided naloxone via a physician's prescription for a patient taking high-dose prescription opioids	○	○	○	○	○	○	○
Provided naloxone via a physician's prescription for a patient with a history of illicit opioid use	○	○	○	○	○	○	○
Provided naloxone via Alabama's statewide standing order for a patient taking high-dose prescription opioids	○	○	○	○	○	○	○
Provided naloxone via Alabama's statewide standing order for a patient with a history of illicit opioid use	○	○	○	○	○	○	○
Initiated a conversation with a patient or caregiver about the benefits of naloxone	○	○	○	○	○	○	○
Billed a third-party payer for the dispensing of naloxone	○	○	○	○	○	○	○
Notified an individual's physician after naloxone was dispensed	○	○	○	○	○	○	○
Marketed the pharmacy's naloxone services using in-store advertisements like posters, flyers, or bag stuffers	○	○	○	○	○	○	○
Marketed the pharmacy's naloxone services using external media like radio, newspaper, or TV advertisements	○	○	○	○	○	○	○

3. Please indicate the types of naloxone stocked in your pharmacy by checking the appropriate box and enter the approximate number of naloxone prescriptions dispensed in the past 3 months.

	In the past 3 months, which types of naloxone did you stock at your pharmacy? Check all that apply.	How many naloxone prescriptions did you dispense in the past 3 months?
	Check if stocked in past 3 months	Enter number dispensed in past 3 months
Nasal spray (Narcan)	☐	_____
Auto-injector (Evzio)	☐	_____
Vial for intramuscular injection + syringe	☐	_____
Pre-filled syringe +/- mucosal atomizer	☐	_____

PART 6:
FACTORS MOTIVATING YOU TO PARTICIPATE IN NALOXONE SERVICES OR TRAINING (O1)

---

1. On a scale of 1 to 7, please rate the extent to which you agree or disagree with the following statements regarding your **MOTIVATION TO PARTICIPATE** in naloxone services or training at your pharmacy, with 1 being strongly disagree and 7 being strongly agree.

Factors motivating my participation in naloxone services or training include:

	Strongly disagree	Disagree	Somewhat disagree	Neither agree nor disagree	Somewhat agree	Agree	Strongly Agree
Being perceived as a pharmacy leader	○	○	○	○	○	○	○
Advancing the profession of pharmacy	○	○	○	○	○	○	○
Improving the image of my pharmacy in the community	○	○	○	○	○	○	○
Fulfilling my duty and obligation as a pharmacist to help patients	○	○	○	○	○	○	○
Improving the health and well-being of my patients	○	○	○	○	○	○	○
Preventing possible opioid overdose deaths in my community	○	○	○	○	○	○	○

Avoiding losing the status and respect of my professional peers	○	○	○	○	○	○	○
Avoiding being perceived as an uncompassionate and uncaring organization	○	○	○	○	○	○	○
Avoiding harm to my patients	○	○	○	○	○	○	○
Complying with a professional manager or decision-maker's request	○	○	○	○	○	○	○
Avoiding potential loss of patients to pharmacy competitors	○	○	○	○	○	○	○
Avoiding future economic repercussions related to patient overdose	○	○	○	○	○	○	○
Preventing healthcare expenditures related to overdose treatment in my community	○	○	○	○	○	○	○
Providing an additional revenue stream for my pharmacy	○	○	○	○	○	○	○
Providing a competitive advantage over other pharmacies	○	○	○	○	○	○	○
Saving staff time contacting physicians or other providers to prescribe naloxone	○	○	○	○	○	○	○
Improving the technical expertise and job skills of myself / my pharmacy staff	○	○	○	○	○	○	○

PART 7
PHARMACY AND PHARMACIST CHARACTERISTICS (O1)

---

1. Please answer the following questions about yourself by entering whole numbers in the spaces below:

○ Your name (First and Last): _____

○ Your age in years: _____

○ Years practicing pharmacy: _____

○ Years at current pharmacy site: _____

----

2. Please indicate your sex:

◯ Male

◯ Female

◯ Prefer not to answer

---

3. With which race do you most closely identify?

◯ White / Caucasian

◯ Black / African American

◯ Asian or Pacific Islander

◯ Native American or Alaska Native

◯ Other

◯ Prefer not to answer

---

4. What is your ethnicity?

◯ Hispanic origin

◯ Non-Hispanic origin

◯ Prefer not to answer

---

5. What is your level of education? Check all that apply.

☐ BSPharm

☐ PharmD

☐ Masters degree

☐ PhD

☐ Residency

☐ Fellowship

☐ Other. Please specify: _____

---

6. What is your job title?

○ Staff pharmacist

○ Pharmacist-in-charge or pharmacy manager

○ Pharmacy owner/partner

○ Other. Please specify: _____

---

7. Which description most closely matches your pharmacy practice site?

○ Single-store independent pharmacy

○ Multi-store independent pharmacy

○ Chain pharmacy

○ Mass merchandiser

○ Grocery

○ Clinic

○ Other. Please specify: _____

---

8. Please answer the following questions about your pharmacy site by typing a number in the spaces below. FTE = Full-time equivalent of 40 hrs/week.

○ How many FTEs of staff pharmacists does your pharmacy employ? Enter a whole number or fraction, such as "2" or "2.5": _____

○ How many FTEs of technicians are employed?: _____

○ What is the average prescription volume per **day**?: _____

---

9. On average, how many opioid prescriptions does your pharmacy dispense **per day**? Please enter a number below

Average number of opioid prescriptions dispensed **per day**: _____

Naloxone: A Guide for Alabama Community Pharmacists

DEVELOPED AS PART OF A DISSERTATION PROJECT AT

AUBURN UNIVERSITY HARRISON SCHOOL OF PHARMACY

LINDSEY HOHMANN, PHARMD | PHD CANDIDATE

AUBURN UNIVERSITY HARRISON SCHOOL OF PHARMACY

DEPARTMENT OF HEALTH OUTCOMES RESEARCH & POLICY

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Disclosures & Conflicts of Interest

2

► Dr. Lindsey Hohmann has no conflicts of interest to disclose.

► Dr. Marilyn Bulloch is a *Pharmacy Times* contributor.

► Dr. Kimberly Braxton-Lloyd has no conflicts of interest to disclose.

► Mr. Denton (Beau) Scott has no conflicts of interest to disclose.

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Naloxone: A Guide for Alabama Community Pharmacists Learning Objectives

3

► Describe naloxone administration techniques and current policies in Alabama

► Discuss strategies to market naloxone and integrate naloxone services into the dispensing workflow

► Discuss strategies to approach and communicate with patients about receiving naloxone

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Naloxone: A Guide for Alabama Community Pharmacists Modules

4

► Module 1: Naloxone Basics
  ► *0001-0000-18-066-L01-P (0.05 CEUs)*
  ► *Presented by Dr. Marilyn Bulloch, PharmD*

► Module 2: Implementation Strategies
  ► *0001-0000-18-067-L01-P (0.05 CEUs)*
  ► *Presented by Dr. Kimberly Braxton-Lloyd, PharmD*

► Module 3: Communication Strategies
  ► *0001-0000-18-068-L01-P (0.05 CEUs)*
  ► *Presented by Mr. Denton (Beau) Scott*

► Question and Answer Session

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Module 1
Naloxone Basics

PRESENTED BY:

MARILYN BULLOCH, PHARMD, BCPS, FCCM

ASSOCIATE CLINICAL PROFESSOR

AUBURN UNIVERSITY HARRISON SCHOOL OF PHARMACY

DEPARTMENT OF PHARMACY PRACTICE

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Module 1 Learning Objectives

At the end of this module, you will be able to:

1. Describe naloxone's mechanism, onset, and duration of action
2. Discuss legal issues surrounding pharmacy-based naloxone provision in Alabama
3. Describe how different naloxone devices work

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Assessment Question 1

1. How long does naloxone take to have an effect?
   a. 2-5 minutes
   b. 6-10 minutes
   c. 11-20 minutes
   d. 21-40 minutes

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Assessment Question 2

▶ The effect of naloxone is shorter than the effect of heroin or methadone.
   a. True
   b. False

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347

The Current Opioid Landscape

Opioid Misuse is a Major Public Health Issue in the United States

▶ 190 million prescriptions for opioid pain relievers written in 2017

▶ 2 million people non-medically dependent on opioid pain relievers in 2014

▶ 17,000 die annually due to prescription opioid overdose
  ▶ As many as 46 people per day
  ▶ Methadone, hydrocodone, oxycodone commonly implicated

National Overdose Deaths
Number of Deaths Involving Opioids
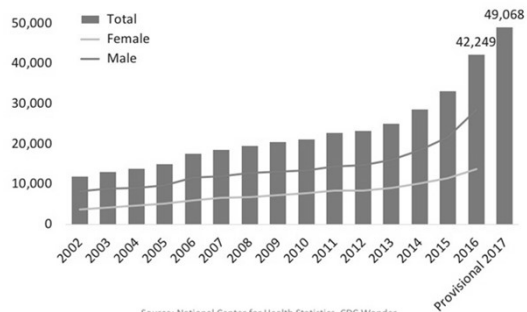
Source: National Center for Health Statistics, CDC Wonder

Rx vs Illicit Opioid Overdose Deaths

▶ Prescription opioids account for a relatively small proportion of overdose deaths overall
  ▶ **Ultra-potent illicit opioids** like fentanyl are a major factor in the current overdose crisis
▶ As pharmacists, we can...
  ▶ Protect our patients using prescription opioids
  ▶ Be mindful of diversion & misuse
  ▶ Be aware that some patients may turn to illicit opioids when faced with decreased prescription availability
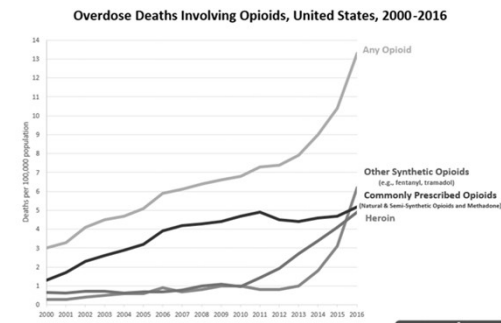
Overdose Deaths Involving Opioids, United States, 2000-2016

Opioid Overdose Deaths are Increasing in Alabama

- Alabama has the highest rate of opioid prescribing in the U.S.
  - 120 prescriptions per 100 people per year

- Opioid overdose deaths in AL increased 23% from 2015-2016

- Opioid overdose deaths throughout the U.S. reached 13.3 / 100,000 in 2016
  - 7.5 in AL
  - 15.4 in Jefferson County, AL

Adapted from National Institute on Drug Abuse (NIDA)
https://www.drugabuse.gov/drugs-abuse/opioids/opioid-summaries-by-state/alabama-opioid-summary

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Treatment and Prevention

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Pain Management & Prescribing

- Centers for Disease Control and Prevention (CDC) Guideline for Prescribing Opioids for Chronic Pain, March 2016
  - Purpose: guide prescribers in outpatient treatment of chronic, non-cancer pain (recommendations, NOT regulations)
  - Opioid doses ≥50 morphine milligram equivalents (MME)/day increase risk of overdose by 2-fold

Adapted from CDC
www.cdc.gov/drugoverdose/prescribing/guideline.html

1. Use non-pharmacologic or non-opioid therapy as first-line
2. Establish goals of treatment
3. Discuss risks and benefits with the patient
4. Use the lowest opioid dose possible and be cautious if increasing the dose to ≥ 50 morphine milligram equivalents (MME) per day; doses over 90 MME/day are not recommended
5. Use immediate release formulations instead of extended release when initiating opioid therapy
6. In cases of acute pain, use short durations of 3-7 days
7. Evaluate benefits and harms to the patient within 1-4 weeks of initiating opioid therapy with follow-ups at least every 3 months thereafter
8. Use strategies to mitigate risk, such as offering naloxone to those on high doses of opioids (over 50 MME/day) or with concurrent benzodiazepine prescriptions
9. Review Prescription Drug Monitoring Program (PDMP) data before prescribing opioids and at least every 3 months
10. Use urine drug testing before initiating opioid therapy and at least annually
11. Avoid prescribing opioids together with benzodiazepines
12. Offer treatment for opioid use disorder, such as medication-assisted treatment (MAT) combining buprenorphine or methadone with behavioral therapy

---

MME Conversions

1. Calculate the total amount of each opioid per day
2. Convert each to MME
3. Add to get the total daily MME

- Precautions:
  - Potential for incomplete cross-tolerance – start at lower dose if switching opioid therapy
  - Methadone & fentanyl conversion factors

Adapted from
www.cdc.gov/drugoverdose/prescribing/guideline.html

OPIOID (doses in mg/day except where noted)	CONVERSION FACTOR
Codeine	0.15
Fentanyl transdermal (in mcg/hr)	2.4
Hydrocodone	1
Hydromorphone	4
Methadone	
1-20 mg/day	4
21-40 mg/day	8
41-60 mg/day	10
≥ 61-80 mg/day	12
Morphine	1
Oxycodone	1.5
Oxymorphone	3

Risks & Signs of Addiction/Opioid Use Disorder

- Risks
  - Rural areas or low income
  - History of mental illness, alcohol, or substance abuse
- Signs
  - Prescriber from outside the local area or outside scope of practice
  - High dose/quantity
  - Cash-pay only
  - Asking for early fills
  - Multiple prescribers/pharmacies

Adapted from: Centers for Disease Control and Prevention (CDC) https://www.cdc.gov/drugoverdose/opioids/prescribed.html & Prescribe to Prevent http://prescribetoprevent.org/pharmacists/pharmacy-basics/

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Treatment for Opioid Use Disorder

- Non-medication related treatment
  - Cognitive behavioral therapy

- Medication Assisted Treatment (MAT)
  - Methadone
  - Buprenorphine (Subutex®) & Buprenorphine/naloxone (Suboxone®)
  - Naltrexone

Adapted from Prescribe to Prevent http://prescribetoprevent.org/pharmacists/pharmacy-basics/

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Risk Factors for Opioid Overdose

- Concurrent opioid prescriptions from multiple providers/pharmacies
- Concurrent high-risk medications like benzodiazepines
- High daily doses of prescription opioids, Ex. ≥50 MME
- Extended release (ER) formulations to treat acute pain
- Comorbid medical conditions affecting lungs/liver/kidney, Ex. COPD

Adapted from CDC https://www.cdc.gov/drugoverdose/opioids/prescribed.html

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Overdose Prevention

- Start low and go slow
  - If switching to a new opioid or re-initiating treatment

- Make sure friends, family, caregivers are educated on how to recognize and respond to an overdose

- Don't take opioids at the same time as other substances like alcohol or high-risk medications like benzodiazepines

- Lock up or keep unused/expired opioid prescriptions out of reach of children/pets/visitors

Adapted from Prescribe to Prevent http://prescribetoprevent.org/pharmacists/pharmacy-basics/

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Prevention Strategies and Policies

► External policies
  ► Prescribing & dispensing regulations
  ► Insurance formulary restrictions
  ► Manufacturer quantity limits & restricted pharmacy allotments

Fink et al, 2018
- PDMP may decrease Rx overdose but increase illicit overdose
- Offer resources to patients with concerning histories

► What you can do
  ► Prescription Drug Monitoring Programs (PDMP's) - https://www.alabamapublichealth.gov/pdmp/index.html
  ► Report suspicious activity to the Board of Medical Examiners or local law enforcement - http://www.albme.org/complaint.html
  ► National Prescription Drug Take-Back Days - https://takebackday.dea.gov/

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Signs of an Opioid Overdose

► Slow or shallow breathing
► Blue lips, hands, or feet
► Loss of consciousness or unresponsiveness
► Deep snoring/choking sounds
► Small (pin-point) pupils
► Pale or clammy skin

Adapted from Nielsen et al, 2016 & Williams et al, 2013

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How to Manage an Opioid Overdose

► Check for responsiveness (yell their name, rub center of chest)
► Call an ambulance (911)
► Administer naloxone
► Check for breathing
► Check for blocked airways (nose and mouth)
► Administer chest compressions or rescue breathing
► Place the person in the recovery position (on their side, mouth clear)
► Stay with the person until emergency responders arrive

Adapted from Nielsen et al, 2016 & Williams et al, 2013

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Naloxone

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351

Slide 25

What is Naloxone?

- Naloxone is an opioid antagonist
  - Reverses effects of an opioid overdose

- Is take-home naloxone (THN) effective?
  - Co-dispensing of naloxone with chronic opioid prescriptions can reduce opioid-related emergency-department (ED) visits by 63% (Coffin et al, 2016)
  - Statewide naloxone access laws are associated with a 14% (p=0.033) reduction in opioid overdose mortality (McClellan et al, 2018)

Naloxone

Opioid receptors on brain

http://prescribetoprevent.org/pharmacists/pharmacy-basics/

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Slide 26
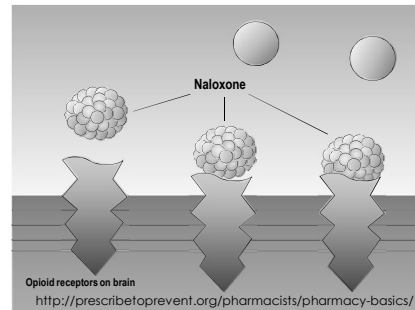
How Does it Work?

Onset of action	• 2-5 minutes
Duration of action	• About 1 hour (30-90 minutes) • Shorter than the effect of heroin or methadone
Site of administration	• Outside of thigh/upper arm (IM) • Intranasal
If first dose has no effect in 2-3 minutes	• Give 2nd dose

Adapted from Nielsen et al, 2016; Williams et al, 2013; & PrescribetoPrevent.org

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Slide 27

Commercially Available Naloxone Dosage Forms

Injection vial or Prefilled syringe +/- mucosal atomizer -Available as generic

Nasal spray -Branded only (Narcan®)

Auto-injector -Branded only (Evzio®)

Shelf-life: 12-18 months

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Slide 28

Acquisition Cost

	Injection Vial or Prefilled Syringe +/- Atomizer (Generic)	Nasal Spray (Narcan®)	Auto-injector (Evzio®)
Dosage	0.4mg/mL (vial) 1mg/mL (PFS)	4mg (2-pack)	2mg (2-pack)
Route	IM or IN	IN	IM or subQ
Label Status	FDA-approved (IM) Off-label (IN)	FDA-approved	FDA-approved
WAC Cost	~$50	$125	$3,750

Adapted from Carpenter et al, 2016 & prescribetoprevent.org/wp2015/wp-content/uploads/Naloxone-product-chart.17_04_14.pdf

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Side Effects of Administering Naloxone

▶ Naloxone is contraindicated in those with an allergy

▶ Otherwise, the main consequence of naloxone administration is symptoms of opioid withdrawal
  ▶ Nervousness, restlessness, irritability
  ▶ Body aches
  ▶ Dizziness or weakness
  ▶ Diarrhea, stomach pain, nausea
  ▶ Fever, chills, goose bumps
  ▶ Sneezing or runny nose

Adapted from https://www.samhsa.gov/medication-assisted-treatment/treatment/naloxone

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Addressing Naloxone Myths

▶ Media stories claim that fentanyl and other ultra-potent opioids are resistant to naloxone
  ▶ These opioids are **NOT resistant to naloxone**
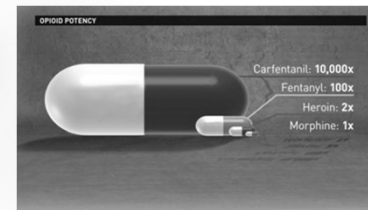
Adapted from Operation Naloxone http://sites.utexas.edu/naloxone/fentanyl/ & Harm Reduction Coalition https://harmreduction.org/blog/fentanyl-exposure/

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Are Community Pharmacies Dispensing Naloxone?

▶ Naloxone dispensing in community pharmacies increased 1170% from 2013 to 2015 (Jones et al, 2013)

▶ 50.6% of pharmacies in California have intranasal naloxone in stock (Puzantian et al, 2018)
  ▶ 52.3% chain vs 31% independent pharmacies (p=0.03)

▶ 69.4% of chain pharmacists in Texas stock some form of naloxone and dispense using a standing order (Evoy et al, 2018)

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What's Legal?

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Naloxone Access Laws

Naloxone Access in Community Pharmacies

Based on data collected by NASPA (updated January 2018)

Labels:
- Statewide Protocol/Pharmacist Prescribing
- Statewide Standing Order
- Dispense without a prescription
- Standing Order
- None

NASPA

https://naspa.us/resource/naloxone-access-community-pharmacies/

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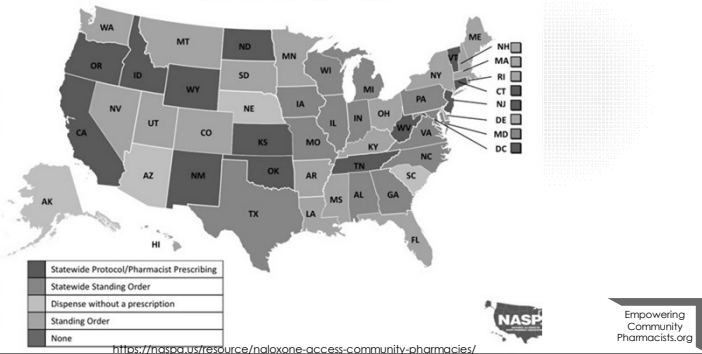
Good Samaritan Laws

6/30/17 Do dispensers have immunity from <u>civil liability</u> for prescribing, dispensing or distributing naloxone to a layperson?

Labels
- (41) Yes
- (10) No
- No data

http://pdaps.org/datasets/laws-regulating-administration-of-naloxone-1501695139

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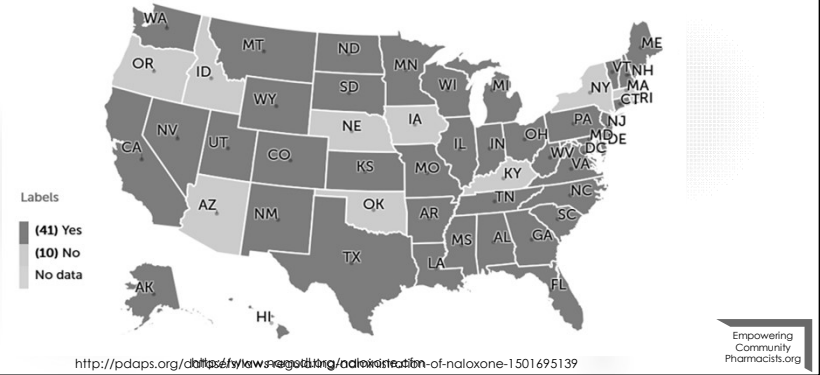
Naloxone Dispensing Laws in Alabama

▶ HB208 – June 12, 2015

  ▶ Allows pharmacists to dispense naloxone via state-wide standing order

  ▶ Protects pharmacists from civil/criminal liability

Ala. Code § 20-2-280

"(b) A physician…or dentist…may directly or by standing order prescribe, and a pharmacist…may dispense, an opioid antagonist to either of the following:
(1) An individual at risk of experiencing an opiate-related overdose.
(2) A family member, friend, member of a fire department…"

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Alabama's State-wide Standing Order

Alabama Department of Public Health

III.   **Pharmacist Actions**

- Provide basic instruction on recognition of opioid overdose, calling 911, rescue breathing, and administration of naloxone as described in the Standing Order.
- Dispense naloxone kit and explain contents to the individual.
- Counseling: Offer information on risk factors for opioid overdose, overdose prevention measures, risk and recognition of addiction, and resources for mental health and addiction treatment services.
- Have client complete and sign Client Form (page 6) attesting to need for naloxone, receipt of instructions, and offer of counseling. If bulk dispensing to a law enforcement agency, fire department, rescue squad, or volunteer fire department, have the agency representative complete and sign the Agency Form (page 7).
- Keep a record of all clients who have received naloxone via this standing order.

Scott Harris, M.D., M.P.H.
State Health Officer
NPI Number: 1992713408
License Number: MD.16614

Date 3/8/18

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354

Naloxone Client Form

1. Check one:

a)

b)
at risk

Write i
kept c

2. ___ I have received information on how to recognize and respond to a possible opioid overdose.

3. ___ I have received basic instructions on how to administer naloxone.

4. ___ I have been offered information/counseling on risk factors for opioid overdose, overdose prevention measures, risk and recognition of addiction, and resources for mental health and addiction treatment services.

I understand that I may administer naloxone to another individual if I have a good faith belief that the individual is experiencing an opioid-related overdose, and if I exercise reasonable care in administering the naloxone.

Signature: _____ Date Signed: _____

Print Name: _____ Date of Birth: _____

27

38

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Nasal Spray (Narcan®)

39

Remove NARCAN Nasal Spray from the box.
Peel back the tab with the circle to open the NARCAN Nasal Spray.

Hold the NARCAN nasal spray with your thumb on the bottom of the plunger and your first and middle fingers on either side of the nozzle.

Gently insert the tip of the nozzle into either nostril.
- Tilt the person's head back and provide support under the neck with your hand. Gently insert the tip of the nozzle into **one nostril**, until your fingers on either side of the nozzle are against the bottom of the person's nose.

Press the plunger firmly to give the dose of NARCAN Nasal Spray.
- Remove the NARCAN Nasal Spray from the nostril after giving the dose.

Adapted from: https://www.narcan.com/patients/how-to-use-narcan
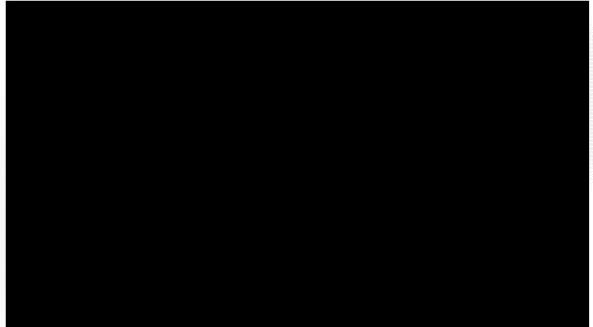
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Nasal Spray (Narcan®)

40

Adapted with permission from OperationNaloxone.org https://youtu.be/RVf1dyRrgHs

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Auto-injector (Evzio®)

Using EVZIO: Administration steps

1 Pull EVZIO from the outer case.

Do not go to Step 2 [Do not remove the **red** safety guard] until you are ready to use EVZIO. **If you are not ready to use EVZIO, put it back in the outer case for later use.**

2 Pull off the **red** safety guard.

To reduce the chance of an accidental injection, do not touch the **black** base of the auto-injector, which is where the needle comes out. If an accidental injection happens, get medical help right away.

Note: The **red** safety guard is made to fit tightly. **Pull firmly to remove. Do not replace the red safety guard after it is removed.**

3 Place the **black** end of EVZIO against the outer thigh, through clothing, if needed. **Press firmly** and hold in place for 5 seconds. If you give EVZIO to an infant less than 1 year old, pinch the middle of the outer thigh before you give EVZIO and continue to pinch while you give EVZIO.

Note: EVZIO makes a distinct sound [click and hiss] when it is pressed against the thigh. This is normal and means that EVZIO is working correctly. Keep EVZIO firmly pressed on the thigh for 5 seconds after you hear the click and hiss sound. The needle will inject and then retract back up into the EVZIO auto-injector and is not visible after use.

4 **After using EVZIO, get emergency medical help right away.** If symptoms return after an injection with EVZIO, an additional injection using another EVZIO may be needed. Give additional injections using a new EVZIO auto-injector every 2 to 3 minutes and continue to closely watch the person until emergency help is received. **EVZIO does not take the place of emergency medical care.**

EVZIO cannot be reused. After use, place the auto-injector back into its outer case. Do not replace the **red** safety guard.

For more detailed information on how to use EVZIO, click here.

Adapted from https://www.evzio.com/patient/how-to-use-evzio/

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Auto-injector (Evzio®)
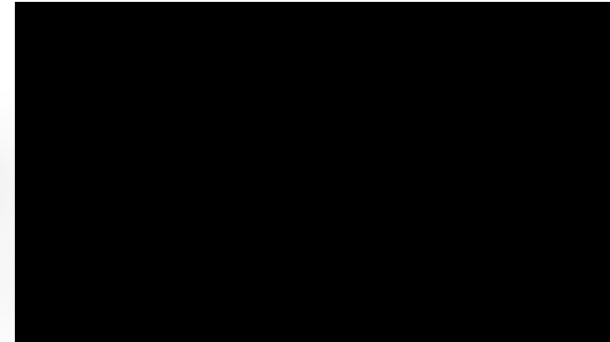
Adapted from Veterans Affairs (VA) https://youtu.be/-DQBCnrAPBY

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Resources

- Alabama Department of Public Health (Standing Order): https://www.alabamapublichealth.gov/pharmacy/naloxone-dispensing.html
- CDC Opioid Guideline Mobile App: https://www.cdc.gov/drugoverdose/prescribing/app.html
- Prescribe to Prevent: http://prescribetoprevent.org/
- Substance Abuse and Mental Health Services Administration (SAMHSA): https://www.samhsa.gov/medication-assisted-treatment/treatment/naloxone
- Veterans Affairs (VA) Demonstration Video: https://youtu.be/0w-us7fQE3s

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Additional Naloxone Administration Examples – All Dosage Forms
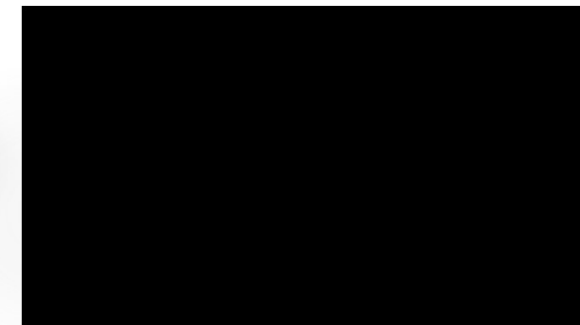
Used with permission from OperationNaloxone.org https://youtu.be/RVf1dyRrgHs

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Assessment Question 1

1. How long does naloxone take to have an effect?
   a. 2-5 minutes
   b. 6-10 minutes
   c. 11-20 minutes
   d. 21-40 minutes

Assessment Question 2

▶ The effect of naloxone is shorter than the effect of heroin or methadone.
   a. True
   b. False

Module 2
Implementation Strategies

PRESENTED BY:

KIMBERLY BRAXTON-LLOYD, PHARMD

PROFESSOR

DIRECTOR, AUBURN UNIVERSITY PHARMACEUTICAL CARE CENTER (AUPCC)

AUBURN UNIVERSITY HARRISON SCHOOL OF PHARMACY

DEPARTMENT OF PHARMACY HEALTH SERVICES

Module 2 Learning Objectives

At the end of this module, you will be able to:

1. Describe how to create a naloxone protocol and set service goals
2. Discuss naloxone marketing, patient identification, documentation and follow-up strategies
3. List resources to integrate naloxone services into the dispensing workflow

Assessment Question 1

► Personal selling is an effective way to market naloxone services in your pharmacy.
   a. True
   b. False

Role and Scope

Pharmacists and Harm Reduction

► Clean needle or syringe programs
   ► States with clean needle or syringe programs in pharmacies are associated with 3 times lower odds of HIV or HCV diagnosis (Neaigus et al, 2008)

► Supervised methadone programs
   ► Supervised methadone programs in pharmacies were well-received by patients due to local access and flexible hours of operation (Luger et al, 2000)

► Buprenorphine/naloxone programs
   ► Supervised buprenorphine/naloxone programs via pharmacist-physician collaborative practice showed 100% patient retention at 6 months and 88% urine toxicology screens negative for opioids (DiPaula et al, 2015)

Pharmacists and Naloxone Services

► Community pharmacy-based naloxone services have been studied for several years

   ► Injection drug users in Rhode Island were in-support of pharmacy-based naloxone services (Zaller et al, 2013)

   ► Collaborative practice agreements and standing orders have increased patient access to naloxone via pharmacies and enabled expansion of pharmacy-based naloxone services (Green et al, 2015 and Lim et al, 2016)

   ► Distribution of the naloxone statewide standing order in New Mexico was associated with a 9-fold increase in Medicaid claims for naloxone from community pharmacies (Morton et al, 2017)

Pharmacists' Preparedness to Dispense Naloxone

53

- ▶ Pharmacists are generally supportive of naloxone services
- ▶ However, some barriers need to be overcome

Barriers				
Lack of time	Lack of training	Uncertainty in identifying & approaching patients	Trouble with reimbursement	Difficulty communicating with prescribers
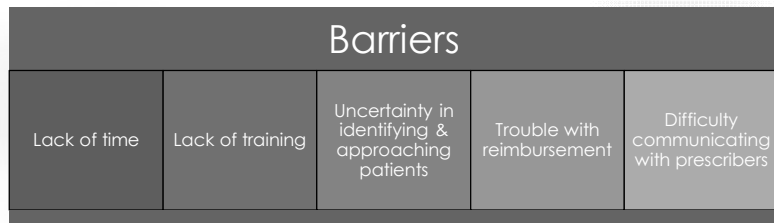
Adapted from Watson et al, 2012

54

Implementing Naloxone Services in YOUR Pharmacy
STRATEGIES TO OVERCOME BARRIERS

Why Are Naloxone Services Important for Your Pharmacy?

55

- ▶ Additional source of revenue
- ▶ Patient expectations
- ▶ Personnel expectations

- ▶ Sustain your pharmacy business in an increasingly competitive environment

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Structures and Processes

56

- ▶ Plan
  - ▶ Structures: building/enhancing a naloxone service

- ▶ Do
  - ▶ Processes: performing naloxone service activities

- ▶ Check-Act
  - ▶ Evaluating and improving for next year

http://1.bp.blogspot.com/-RFddu7uvqgo/UaTtQ7Emwil/AAAAAAAAB24/3b13aueAGnk/s1600/PDCA_13950312_s.jpg

Planning Stage

Structures: Building a Naloxone Service

1. Develop Formal Pharmacy Protocols/Procedures
2. Optimize Workflow
3. Ensure Adequate Resources/Technology
4. Create a Program Evaluation & Budget Plan

---

1. Develop Formal Pharmacy Protocols & Procedures

- Prepare an action plan
- Set objectives/goals
- Create a procedure for how to identify eligible patients
- Prepare an outreach/marketing plan

- A Gantt Chart is a useful organizational tool for this planning stage

---

Gantt Chart

GANTT CHART TEMPLATE

TASK NAME	START DATE	END DATE	DURATION (WORK DAYS)	TEAM MEMBER	PERCENT COMPLETE
First Sample Project					
Write Landing Page Copy	1/5	1/8	2	Nathan	100%
			0	Meredith	80%
Review Landing Page Design	1/11	1/16	4	Brandon	60%
Build Landing Page	1/14	1/19	5	Michael	40%
Code Review Landing Page	1/17	1/21	3	Rachel	20%
Promote Landing Page	1/20	1/23	2	Annie	10%
Second Sample Project					
Write Promotional Email	2/5	2/8	4	Nathan	100%
Design Promotional Email	2/8	2/13	4	Meredith	80%
Send Promotional Email to Contacts	2/11	2/16	5	Michael	60%
Analyze Results of Email Campaign	2/14	2/23	8	Annie	40%
Third Sample Project					
Plan Agenda for Team Meeting	3/5	3/8	4	Rachel	100%
Reserve Room and Resources for Meeting	3/8	3/13	4	Michael	80%
Finalize Team Presentation	3/11	3/16	5	Brandon	60%
Review & Approve Presentation	3/14	3/19	4	Meredith	40%
Create Invitations for Meeting	3/17	3/21	3	Annie	20%

Gantt Chart w % Complete | Basic Gantt Chart | **Manual Chart**

https://www.teamgantt.com/free-gantt-chart-excel-template

360

Setting Goals and Objectives

- SMART objectives
  - S=specific
  - M=measurable
  - A=achievable
  - R=relevant/realistic
  - T=time-bound

- Examples:
  - Goal (broad statement): To increase the number of naloxone prescriptions dispensed in our pharmacy.
  - Objective: Each month, 10 patients receiving an opioid prescription from our pharmacy will be asked about receiving naloxone.

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Creating Risk Assessment, Dispensing, & Counseling Protocols

Risk Assessment	Prescription Template	Standing Order

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2. Optimize Workflow

Choose a leader/champion
- Facilitate team members' tasks & communicate with all staff members

Decide each person's role and delegate tasks. Who will...
- Assess patients' naloxone status?
- Complete/file paperwork, including standing order?
- Process payments/billing?
- Hand out naloxone flyers/brochures?
- Counsel naloxone recipients (student interns)?

Arrange staff schedules & adjust prescription workflow if needed
- Naloxone services: time of the day, day of the week offered? Appointment vs walk-in?
- Start small – limit to certain days/times

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3. Ensure Adequate Resources/Technology

- Seek management/owner support
  - Communicate the social and economic benefits for the pharmacy business
  - Share action plan, Gantt Chart, and objectives
  - Share the plan for continuous evaluation and improvement in the coming year(s)

- Access Alabama's Prescription Drug Monitoring Program (PDMP)
  - Available at the Alabama Department of Public Health (ADPH)
  - https://www.alabamapublichealth.gov/pdmp/index.html

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4. Create a Program Evaluation Plan

▶ Create a plan to continuously evaluate and improve naloxone services
  ▶ Assess whether objectives were met
  ▶ Use results to adjust the plan for the coming year(s)

Implementation Stage

Processes: Performing Naloxone Service Activities

1. Maintain Workflow
2. Identify Patients
3. Dispense and Counsel
4. Market the Service

---

1. Maintain Workflow

Conduct staff meetings

Keep at least one dosage form of naloxone in stock

Bill naloxone via **recipients'** insurance or cash

• Some dosage forms covered by insurance
  • Medicaid (nasal spray)
  • BlueCross BlueShield (BCBS) of Alabama (nasal spray)
• Coupons available for some dosage forms
  • GoodRx https://www.goodrx.com/naloxone
• Check patient assistance programs
  • Kaleo, Inc. Patient Assistance Program (auto-injector)
    https://www.rxassist.org/pap-info/company-detail?CmpId=690

Adapted from https://www.al.com/news/index.ssf/2018/03/bluecross_blueshield_changing.html and
https://www.narcan.com/patients/how-to-get-narcan

2. Identify Patients

Targeted approach	Universal approach
• Identify eligible patients via medication profile, drop-off screening, medical history, non-prescription consultations • Target high dose opioid (≥50 MME), concomitant high-risk medications (benzodiazepines), high-risk comorbid conditions (ex. COPD, asthma)	• Recommend naloxone to every patient, every opioid prescription, every time • Reduces perception of targeting/stigma

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3. Dispense and Counsel

Wait and see approach	Proactive approach
• Wait to receive a physician's prescription	• Identify and approach eligible patients to provide naloxone using Alabama's statewide standing order

► Educate patients AND family, friends, caregivers
  ► How to recognize/response to opioid overdose
  ► Risk factors for overdose/addiction, overdose prevention, addiction treatment resources
  ► How to administer naloxone
► Document and follow up

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Documentation and Follow-Up

► Patients or caregivers
  ► Refer **>>** Follow-up call
  ► Not in stock **>>** Order **>>** Follow-up call
  ► Hesitant **>>** Document **>>** Follow-up at next visit

► Prescribers
  ► Dispense **>>** Notify via <u>ready-made fax form</u>

► Facilitates formation of trusting relationships and repeat business

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4. Market the Service

► Personal selling
  ► Initiate a conversation with the patient, friend, family member or caregiver about the benefits of naloxone
  ► Healthcare provider recommendations are positively associated with increased patient uptake of services (Gilkey, 2016)

► In-store media (intercom announcement, bag stuffers, posters, flyers)
► External media (radio, TV announcements)
► Community outreach (health fairs)

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Create a Culture of Safety
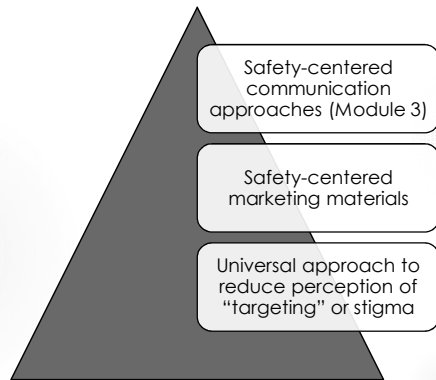
Safety-centered communication approaches (Module 3)

Safety-centered marketing materials

Universal approach to reduce perception of "targeting" or stigma

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Resources

▶ In-store posters:
https://www.cdc.gov/drugoverdose/prescribing/posters.html &
http://prescribetoprevent.org/patient-education/materials/
▶ Patient handouts:
https://www.cdc.gov/drugoverdose/patients/materials.html
▶ Gantt Chart template: https://www.teamgantt.com/free-gantt-chart-excel-template
▶ SAMHSA Behavioral Health Treatment Services Locator:
https://findtreatment.samhsa.gov/
▶ Tips for writing effective communications to prescribers:
http://www.thethrivingpharmacist.com/2015/04/14/writing-effective-communications-to-prescribers/
▶ Prescriber fax template:
https://drive.google.com/file/d/1xf7qJta7nyucpUXpNnf0uiV4WJ70PfJd/view?usp=sharing

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Assessment Question 1

▶ Personal selling is an effective way to market naloxone services in your pharmacy.

a. True
b. False

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Module 3
Communication Strategies

PRESENTED BY:

DENTON (BEAU) SCOTT, MA

DOCTORAL STUDENT, CLINICAL PSYCHOLOGY

INTERN STAFF CLINICIAN

STUDENT COUNSELING AND PSYCHOLOGICAL SERVICES (SCPS)

AUBURN UNIVERSITY

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Module 3 Learning Objectives

At the end of this module, you will be able to:

1. Describe how motivational interviewing techniques can be used to approach and communicate with patients about naloxone
2. Locate resources to use when counseling patients about naloxone
3. State "Go-To" phrases to recommend naloxone

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Assessment Question 1

▶ Which of the following is NOT a key element of motivational interviewing (MI)?
   a. Compassion
   b. Autonomy
   c. Paternalism
   d. Collaboration

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The Approach

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The Patient Encounter

▶ Brief education of 5 minutes is sufficient to significantly increase patient knowledge about opioid overdose and naloxone administration (p<0.001) (Behar et al, 2014)
▶ Patients are comfortable discussing opioid use and naloxone with their primary care physicians (Han et al, 2017)
▶ However, patient resistance is a common barrier encountered by pharmacists

▶ Methods to reduce patient resistance to receiving naloxone in the pharmacy:
   ▶ Use a universal approach
   ▶ Use safety-centered language
   ▶ Use elements of motivational interviewing (MI)

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Types of Prevention Strategies

Universal prevention strategies are designed to reach the entire population, without regard to individual risk factors and are intended to reach a very large audience.

- Example: Everyone with access to opioids, including patients, family members, and caretakers.

Selective prevention strategies target subgroups of the general population that are determined to be at risk for a condition.

- Example: Patients who have been using opioids for an extended period of time and/or at higher doses.

Indicated prevention interventions identify individuals who are experiencing early signs of a condition, or already have the condition.

- Example: Patients who show signs of opioid use disorder, have a history of overdosing, or misuse other substances

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Benefits of a Universal Approach

► Cast a wide net

► Normalize conversations about risks and benefits of opioids and naloxone

► Create Culture of Safety (and NOT Culture of Suspicion)

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Creating a Culture of Safety

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Creating a Culture of Safety

► Safety-centered language can help to reduce patient resistance to receiving naloxone

Culture of Safety	Culture of Suspicion
• "Opioids are risky for everyone who uses them" • "Anyone can experience an accidental overdose" • "We are making an effort to reach out to as many patients as possible"	• "You seem like someone who might be at risk" • "You seem like the type of person who could overdose" • "I am targeting the patients I am most worried about"

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Using Elements of Motivational Interviewing (MI)

What is Motivational Interviewing?

▶ "...a collaborative, person-centered form of guiding to elicit and strengthen motivation for change."

▶ MI is a particular kind of conversation about change.

▶ MI is collaborative (person-centered, partnership, autonomy).

▶ MI is evocative (seeks to call forth the person's own motivation and commitment).

Miller & Rollnick, 2013

The Spirit of MI

▶ Based on four key elements:
  ▶ **Collaboration** between the practitioner and the client.
  ▶ **Evoking** or drawing out the client's ideas about change/choice.
  ▶ Emphasizing the **autonomy** of the client.
  ▶ Practicing **compassion** in the process.

Rollnick & Miller, 1995

Putting Spirit into Practice

Collaboration	• Would it be OK if I talked with you about naloxone? • What can we do to keep you and your family **safe**?
Evoking	• What sorts of concerns or questions do you have about your prescription opioids? • Do you have questions or concerns about naloxone?
Autonomy	• You know what is best for you and your family. • How can I help you make the best decision?
Compassion	• I know these can be difficult topics to talk about. • I know you are doing the best you can to keep yourself and your family **safe**.

Five General Principles of MI

1. Express empathy

2. Develop discrepancy

3. Avoid argumentation

4. Roll with resistance

5. Support self-efficacy

MI Pyramid

Strategies

Principles

Spirit

https://www.dentalcare.com/en-us/professional-education/ce-courses/ce381/components-of-mi

Miller & Rollnick, 1991

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Avoid Argumentation

▶ Patients might have a variety of reasons for declining a conversation about naloxone, or reasons for deciding against taking a prescription.

▶ Arguments about naloxone are likely to be counterproductive.

▶ Resistance from patients is a signal to change strategies and try a different approach.

▶ "Lose the battle, win the war."

Adapted from SAMHSA, 1999

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Rolling with Resistance

▶ One view of resistance is that the client is behaving defiantly.

▶ A more constructive view is simply that client views the situation differently. This requires you to understand your client's perspective and proceed from there.

▶ Adjusting to resistance is similar to avoiding argument in that it offers another chance to express empathy by remaining nonjudgmental and respectful, encouraging the client to talk and stay involved.

▶ Try to avoid evoking resistance whenever possible, and divert or deflect the energy the client is investing in resistance toward positive change.

Adapted from SAMHSA, 1999

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Putting Strategies into Practice

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Rolling with Resistance 1

▶ **Simple reflection**
  ▶ Repeat patient's statement in a neutral form. This acknowledges and validates their concern and can elicit an opposite response.

Client: I really don't think I need to worry about overdosing.

Clinician: You don't think you are at risk.

Adapted from SAMHSA, 1999

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Rolling with Resistance 2

▶ **Amplified reflection**
  ▶ Reflect the client's statement in an exaggerated form, but without sarcasm. This can move the client toward positive change rather than resistance.

Client: I don't know why my family is worried about me overdosing. I use my prescriptions the way my doctor tells me to.

Clinician: So your family has absolutely nothing to worry about?

Adapted from SAMHSA, 1999

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Rolling with Resistance 3

▶ **Double-sided reflection**
  ▶ Acknowledging what the client has said, but add in contrary perspective (ideally based on what client has said in the past).

Client: I don't need to worry about overdosing, I'm just not that kind of person!

Clinician: You don't think you will ever overdose. Although you have said that you know some people are very safe but still accidently overdose...and you worry about them.

Adapted from SAMHSA, 1999

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Rolling with Resistance 4

▶ **Shifting focus**
  ▶ Helping the client shift focus away from obstacles and barriers. You can affirm your client's personal choice and still keep the conversation going.

Client: I am not sure I want to spend the money on naloxone.

Clinician: I understand. We are still talking about the possible benefits of having naloxone. You are not ready to decide if it is right for you.

Adapted from SAMHSA, 1999

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Rolling with Resistance 5

▶ **Agreement with a twist**

    ▶ Agree with the client, but with a twist or change of direction that moves the discussion forward.

Client: Why are you and my daughter so stuck on overdosing? It's not like I have ever misused my medication or overdosed in the past.

Clinician: You've got a good point there, and that's important. You have been safe, and we should pay attention to that. We should focus on strategies that can make sure you continue to be as safe as possible.

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Rolling with Resistance 6

▶ **Reframing**

    ▶ Can be useful when a patient denies any risks or problems. Offers a new and positive interpretation of negative information provided by the client.

Client: My family is always telling me I need to be more careful with my pain pills. It makes me feel like they don't trust me, and that makes me mad.

Clinician: It sounds like your family cares about you and wants to make sure you are safe, although how they say it makes you angry. Maybe we can talk about ways to keep you safe in a more positive and acceptable way.

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Resources

▶ Where to learn more about MI: https://motivationalinterviewing.org/motivational-interviewing-resources

▶ Patient handouts to facilitate the conversation: http://prescribetoprevent.org/pharmacists/pharmacy-basics/

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Additional Resource – Example Patient Encounter
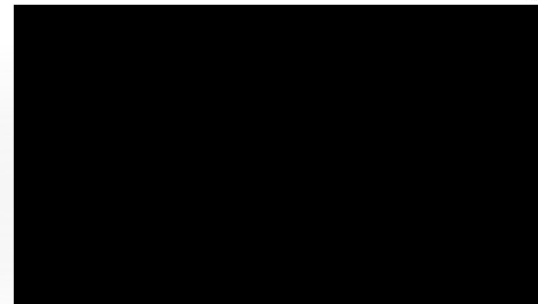
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Assessment Question 1

▶ Which of the following is NOT a key element of motivational interviewing (MI)?

  a. Compassion
  b. Autonomy
  c. Paternalism
  d. Collaboration

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Appendix G
Aim 2 Internal Consistency of Survey Instrument

Construct	KR-20		
	O1	**O2**	**O3**
Knowledge	0.259	0.182	0.835
	Cronbach's Alpha		
	O1	**O2**	**O3**
Intention	0.853	0.904	0.891
Attitudes Overall	0.847	0.853	0.874
Regarding Illicit Opioid Misuse	0.725	0.712	0.632
Regarding Prescription Opioid Misuse	0.820	0.804	0.870
Confidence Overall	0.895	0.883	0.887
Regarding Patient-Oriented Activities	0.915	0.872	0.869
Regarding Business-Oriented Activities	0.815	0.814	0.802
Perceived Barriers Overall	0.891	0.890	0.911
Related to Support and Resources	0.890	0.857	0.898
Related to Business Logistics	0.802	0.853	0.836

Appendix H

Aim 2 Reliability and Validity Analysis: Attitude Scale

Rotated Component Matrix^a		
	Component	
	1	2
On a scale of 1 to 7, please rate the extent to which you agree or disagree with the following statements regarding your ATTITUDES toward pharmacy-based naloxone services, with 1 being strongly disagree and 7 being strongly agree. I believe that: - People who inject illicit opioid drugs visiting my pharmacy would have a damaging effect on business *	.760	-.133
I believe that: - It is appropriate for pharmacists to provide naloxone to people who inject illicit opioids	.653	.292
I believe that: - I feel comfortable supplying naloxone to people who inject illicit opioids	.651	.391
I believe that: - It is appropriate for pharmacists to contact physicians to obtain a naloxone prescription for eligible patients	.608	-.012
I believe that: - It is appropriate for pharmacists to provide naloxone to people who use prescription opioids	.607	.444
I believe that: - I have no sympathy for people who misuse opioids *	.570	.178
I believe that: - Offering naloxone in pharmacies is a good use of time and money	.531	.439
I believe that: - Pharmacists have a role to play in opioid overdose prevention	.485	.462
I believe that: - Supplying naloxone in pharmacies encourages inappropriate use of opioids *	-.230	.786
I believe that: - It is unethical to supply naloxone to people who use opioids *	.120	.704
I believe that: - I feel comfortable supplying naloxone to people who take high-dose opioid prescriptions	.346	.639
I believe that: - It is part of a pharmacists' professional duty to provide naloxone to people who use opioids	.529	.558
I believe that: - Supplying naloxone at the pharmacy will help reduce opioid overdose deaths	.187	.553
I believe that: - Other pharmacists will support my decision to supply naloxone in my pharmacy	.152	.530
I believe that: - People who take high-dose opioid prescriptions visiting my pharmacy would have a damaging effect on business	.336	.343

Extraction Method: Principal Component Analysis.
 Rotation Method: Varimax with Kaiser Normalization.

a. Rotation converged in 3 iterations.

Reverse coded items indicated by *.

Item-Total Statistics

	Scale Mean if Item Deleted	Scale Variance if Item Deleted	Corrected Item-Total Correlation	Squared Multiple Correlation	Cronbach's Alpha if Item Deleted
I believe that: - Supplying naloxone in pharmacies encourages inappropriate use of opioids	74.16	97.086	.285	.474	.853
I believe that: - It is unethical to supply naloxone to people who use opioids	73.42	99.137	.518	.503	.838
I believe that: - It is part of a pharmacists' professional duty to provide naloxone to people who use opioids	74.50	85.492	.698	.537	.822
I believe that: - People who inject illicit opioid drugs visiting my pharmacy would have a damaging effect on business	75.06	94.282	.355	.398	.849
I believe that: - People who take high-dose opioid prescriptions visiting my pharmacy would have a damaging effect on business	74.20	96.609	.425	.432	.841

I believe that: - It is appropriate for pharmacists to provide naloxone to people who inject illicit opioids	74.27	92.643	.575	.687	.832
I believe that: - It is appropriate for pharmacists to provide naloxone to people who use prescription opioids	73.66	96.388	.672	.598	.831
I believe that: - It is appropriate for pharmacists to contact physicians to obtain a naloxone prescription for eligible patients	74.02	97.889	.346	.355	.846
I believe that: - Supplying naloxone at the pharmacy will help reduce opioid overdose deaths	73.97	96.666	.439	.423	.840
I believe that: - Offering naloxone in pharmacies is a good use of time and money	74.47	92.285	.614	.568	.829
I believe that: - Pharmacists have a role to play in opioid overdose prevention	73.53	98.412	.577	.461	.836
I believe that: - Other pharmacists will support my decision to supply naloxone in my pharmacy	73.95	99.410	.385	.375	.843
I believe that: - I feel comfortable supplying naloxone to people who inject illicit opioids	74.97	86.507	.648	.669	.826

	Scale Mean if Item Deleted	Scale Variance if Item Deleted	Corrected Item-Total Correlation	Squared Multiple Correlation	Cronbach's Alpha if Item Deleted
I believe that: - I feel comfortable supplying naloxone to people who take high-dose opioid prescriptions	73.80	94.101	.586	.512	.832

Item-Total Statistics Factor 1

	Scale Mean if Item Deleted	Scale Variance if Item Deleted	Corrected Item-Total Correlation	Squared Multiple Correlation	Cronbach's Alpha if Item Deleted
I believe that: - People who inject illicit opioid drugs visiting my pharmacy would have a damaging effect on business	22.06	16.123	.535	.299	.658
I believe that: - It is appropriate for pharmacists to provide naloxone to people who inject illicit opioids	21.27	18.484	.537	.440	.662
I believe that: - It is appropriate for pharmacists to contact physicians to obtain a naloxone prescription for eligible patients	21.02	20.206	.355	.145	.723
I believe that: - I feel comfortable supplying naloxone to people who inject illicit opioids	21.97	16.316	.551	.463	.650
I believe that: - I have no sympathy for people who misuse opioids	21.06	18.250	.459	.243	.688

Item-Total Statistics Factor 2

	Scale Mean if Item Deleted	Scale Variance if Item Deleted	Corrected Item-Total Correlation	Squared Multiple Correlation	Cronbach's Alpha if Item Deleted
I believe that: - Supplying naloxone in pharmacies encourages inappropriate use of opioids	53.09	43.134	.433	.395	.817
I believe that: - It is unethical to supply naloxone to people who use opioids	52.36	47.313	.578	.501	.801
I believe that: - It is part of a pharmacists' professional duty to provide naloxone to people who use opioids	53.44	38.948	.668	.507	.784
I believe that: - People who take high-dose opioid prescriptions visiting my pharmacy would have a damaging effect on business	53.14	46.662	.385	.339	.816
I believe that: - It is appropriate for pharmacists to provide naloxone to people who use prescription opioids	52.59	47.197	.573	.402	.801
I believe that: - Supplying naloxone at the pharmacy will help reduce opioid overdose deaths	52.91	45.737	.462	.398	.808
I believe that: - Offering naloxone in pharmacies is a good use of time and money	53.41	43.991	.556	.442	.798

I believe that: - Pharmacists have a role to play in opioid overdose prevention	52.47	47.777	.550	.412	.803
I believe that: - Other pharmacists will support my decision to supply naloxone in my pharmacy	52.89	47.750	.407	.258	.813
I believe that: - I feel comfortable supplying naloxone to people who take high-dose opioid prescriptions	52.73	44.325	.591	.406	.795

Appendix I

Aim 2 Reliability and Validity Analysis: Confidence Scale

Rotated Component Matrix[a]		
	Component	
	1	2
On a scale of 1 to 7, please rate the extent to which you agree or disagree with the following statements regarding your CONFIDENCE in performing naloxone-related activities in your pharmacy, with 1 being strongly disagree and 7 being strongly agree. I am confident in my ability to: - Initiate a conversation with a patient regarding the need for take-home naloxone	.883	.199
I am confident in my ability to: - Communicate with physicians or other providers regarding their patients who may benefit from naloxone	.849	.160
I am confident in my ability to: - Educate patients to recognize opioid overdose	.844	.254
I am confident in my ability to: - Proactively identify patients who would benefit from naloxone	.802	.238
I am confident in my ability to: - Counsel patients on how to safely administer naloxone when indicated	.800	.188
I am confident in my ability to: - Stock naloxone products in my pharmacy	.164	.836
I am confident in my ability to: - Dispense naloxone products in my pharmacy when prescribed by a physician	.038	.818
I am confident in my ability to: - Discuss naloxone cost with patients	.205	.743
I am confident in my ability to: - Correctly bill insurance companies for dispensed naloxone products	.470	.692
I am confident in my ability to: - Dispense naloxone products in my pharmacy using Alabama's statewide standing order	.328	.563
Extraction Method: Principal Component Analysis. Rotation Method: Varimax with Kaiser Normalization.		
a. Rotation converged in 3 iterations.		

Item-Total Statistics

	Scale Mean if Item Deleted	Scale Variance if Item Deleted	Corrected Item-Total Correlation	Squared Multiple Correlation	Cronbach's Alpha if Item Deleted

I am confident in my ability to: - Proactively identify patients who would benefit from naloxone	51.50	64.825	.713	.638	.879
I am confident in my ability to: - Communicate with physicians or other providers regarding their patients who may benefit from naloxone	51.42	64.724	.700	.742	.880
I am confident in my ability to: - Initiate a conversation with a patient regarding the need for take-home naloxone	51.61	62.401	.762	.757	.875
I am confident in my ability to: - Educate patients to recognize opioid overdose	51.34	63.340	.772	.737	.875
I am confident in my ability to: - Counsel patients on how to safely administer naloxone when indicated	51.31	64.377	.676	.632	.882
I am confident in my ability to: - Discuss naloxone cost with patients	51.16	70.039	.524	.456	.892
I am confident in my ability to: - Stock naloxone products in my pharmacy	50.80	70.926	.546	.645	.890
I am confident in my ability to: - Dispense naloxone products in my pharmacy when prescribed by a physician	50.42	75.994	.447	.443	.896

	Scale Mean if Item Deleted	Scale Variance if Item Deleted	Corrected Item-Total Correlation	Squared Multiple Correlation	Cronbach's Alpha if Item Deleted
I am confident in my ability to: - Dispense naloxone products in my pharmacy using Alabama's statewide standing order	51.30	69.164	.518	.398	.893
I am confident in my ability to: - Correctly bill insurance companies for dispensed naloxone products	51.16	64.896	.720	.679	.879

Item-Total Statistics Factor 1

	Scale Mean if Item Deleted	Scale Variance if Item Deleted	Corrected Item-Total Correlation	Squared Multiple Correlation	Cronbach's Alpha if Item Deleted
I am confident in my ability to: - Proactively identify patients who would benefit from naloxone	21.88	23.921	.762	.621	.899
I am confident in my ability to: - Communicate with physicians or other providers regarding their patients who may benefit from naloxone	21.80	23.276	.801	.708	.892
I am confident in my ability to: - Initiate a conversation with a patient regarding the need for take-home naloxone	21.98	22.143	.838	.745	.883
I am confident in my ability to: - Educate patients to recognize opioid overdose	21.72	23.348	.794	.689	.893

	Scale Mean if Item Deleted	Scale Variance if Item Deleted	Corrected Item-Total Correlation	Squared Multiple Correlation	Cronbach's Alpha if Item Deleted
I am confident in my ability to: - Counsel patients on how to safely administer naloxone when indicated	21.69	23.647	.717	.581	.909

Item-Total Statistics Factor 2

	Scale Mean if Item Deleted	Scale Variance if Item Deleted	Corrected Item-Total Correlation	Squared Multiple Correlation	Cronbach's Alpha if Item Deleted
I am confident in my ability to: - Discuss naloxone cost with patients	23.89	11.877	.618	.411	.775
I am confident in my ability to: - Stock naloxone products in my pharmacy	23.53	12.094	.689	.584	.755
I am confident in my ability to: - Dispense naloxone products in my pharmacy when prescribed by a physician	23.16	14.642	.610	.414	.796
I am confident in my ability to: - Dispense naloxone products in my pharmacy using Alabama's statewide standing order	24.03	12.063	.520	.325	.810
I am confident in my ability to: - Correctly bill insurance companies for dispensed naloxone products	23.89	10.702	.688	.522	.753

Appendix J

Aim 2 Reliability and Validity Analysis: Perceived Barriers Scale

Rotated Component Matrix[a]		
	Component	
	1	2
On a scale of 1 to 7, please rate the extent to which you agree or disagree with the following statements regarding BARRIERS to providing naloxone services in your pharmacy, with 1 being strongly disagree and 7 being strongly agree. Factors that make it difficult to provide naloxone services: - The level of general support from other pharmacists for naloxone services is low	.822	.029
Factors that make it difficult to provide naloxone services: - The level of general support from management, corporate, or owners is low	.800	.009
Factors that make it difficult to provide naloxone services: - There are concerns over clientele who might frequent the pharmacy if naloxone services were in place	.800	.173
Factors that make it difficult to provide naloxone services: - There are moral or ethical concerns associated with increasing drug abuse as a result of providing naloxone	.777	.141
Factors that make it difficult to provide naloxone services: - The level of general support from technicians for naloxone services is low	.745	.030
Factors that make it difficult to provide naloxone services: - Counseling patients about naloxone is too time-consuming	.702	.161
Factors that make it difficult to provide naloxone services: - Dispensing naloxone is too time-consuming	.614	.194
Factors that make it difficult to provide naloxone services: - There are not enough pharmacy staff members	.583	.322
Factors that make it difficult to provide naloxone services: - Pharmacy technician staff are not sufficiently trained to implement naloxone services	.582	.058
Factors that make it difficult to provide naloxone services: - It is difficult to identify patients who would benefit from naloxone	.533	.085
Factors that make it difficult to provide naloxone services: - There is community opposition to providing naloxone	.444	.282
Factors that make it difficult to provide naloxone services: - I am unfamiliar with my state's laws and regulations about naloxone	.369	.081
Factors that make it difficult to provide naloxone services: - It is difficult to obtain reimbursement from third-party payers	.043	.834
Factors that make it difficult to provide naloxone services: - The cost of stocking naloxone is too high	.197	.760

Factors that make it difficult to provide naloxone services: - The amount patients have to pay for naloxone is too high	-.105	.724
Factors that make it difficult to provide naloxone services: - There is not enough profit margin	.197	.718
Factors that make it difficult to provide naloxone services: - It is difficult to package or stock the various forms of naloxone	.389	.598
Factors that make it difficult to provide naloxone services: - The level of general support from local physicians is low	.442	.562
Factors that make it difficult to provide naloxone services: - Naloxone expiration dates are too short	.306	.544
Factors that make it difficult to provide naloxone services: - Patients are not interested in receiving naloxone from the pharmacy	-.022	.402
Extraction Method: Principal Component Analysis. Rotation Method: Varimax with Kaiser Normalization.		
a. Rotation converged in 3 iterations.		

Item-Total Statistics

	Scale Mean if Item Deleted	Scale Variance if Item Deleted	Corrected Item-Total Correlation	Squared Multiple Correlation	Cronbach's Alpha if Item Deleted
The level of general support from management, corporate, or owners is low	69.53	312.412	.602	.654	.883
The level of general support from other pharmacists for naloxone services is low	69.16	314.705	.648	.783	.882
The level of general support from technicians for naloxone services is low	69.23	314.500	.583	.676	.884
The level of general support from local physicians is low	68.66	313.277	.631	.595	.883

I am unfamiliar with my state's laws and regulations about naloxone	69.25	329.937	.327	.474	.892
Pharmacy technician staff are not sufficiently trained to implement naloxone services	67.28	320.999	.467	.474	.888
It is difficult to package or stock the various forms of naloxone	68.80	313.022	.579	.607	.884
Naloxone expiration dates are too short	68.44	331.393	.490	.516	.887
The cost of stocking naloxone is too high	68.27	320.770	.507	.663	.886
It is difficult to obtain reimbursement from third-party payers	68.30	324.498	.454	.702	.888
The amount patients have to pay for naloxone is too high	67.89	334.956	.287	.624	.893
There is not enough profit margin	68.08	327.629	.496	.633	.887
Dispensing naloxone is too time-consuming	69.11	323.020	.536	.685	.886
Counseling patients about naloxone is too time-consuming	69.50	319.810	.591	.728	.884
There are not enough pharmacy staff members	68.39	310.115	.587	.516	.884
It is difficult to identify patients who would benefit from naloxone	68.97	326.221	.450	.470	.888
Patients are not interested in receiving naloxone from the pharmacy	67.75	340.508	.188	.455	.896

	Scale Mean if Item Deleted	Scale Variance if Item Deleted	Corrected Item-Total Correlation	Squared Multiple Correlation	Cronbach's Alpha if Item Deleted
There are concerns over clientele who might frequent the pharmacy if naloxone services were in place	68.98	310.301	.690	.753	.881
There are moral or ethical concerns associated with increasing drug abuse as a result of providing naloxone	69.42	312.343	.650	.685	.882
There is community opposition to providing naloxone	69.53	332.253	.447	.468	.888

Item-Total Statistics Factor 1

	Scale Mean if Item Deleted	Scale Variance if Item Deleted	Corrected Item-Total Correlation	Squared Multiple Correlation	Cronbach's Alpha if Item Deleted
The level of general support from management, corporate, or owners is low	40.64	168.520	.711	.572	.875
The level of general support from other pharmacists for naloxone services is low	40.27	170.897	.755	.752	.873
The level of general support from technicians for naloxone services is low	40.34	171.086	.670	.650	.877
The level of general support from local physicians is low	39.77	179.103	.510	.379	.885
I am unfamiliar with my state's laws and regulations about naloxone	40.36	185.789	.335	.307	.894

	Scale Mean if Item Deleted	Scale Variance if Item Deleted	Corrected Item-Total Correlation	Squared Multiple Correlation	Cronbach's Alpha if Item Deleted
Pharmacy technician staff are not sufficiently trained to implement naloxone services	38.39	177.924	.504	.405	.886
Dispensing naloxone is too time-consuming	40.22	180.301	.561	.642	.883
Counseling patients about naloxone is too time-consuming	40.61	176.940	.643	.702	.879
There are not enough pharmacy staff members	39.50	172.254	.570	.452	.883
It is difficult to identify patients who would benefit from naloxone	40.08	182.105	.487	.423	.886
There are concerns over clientele who might frequent the pharmacy if naloxone services were in place	40.09	169.832	.739	.712	.874
There are moral or ethical concerns associated with increasing drug abuse as a result of providing naloxone	40.53	170.983	.706	.660	.876
There is community opposition to providing naloxone	40.64	189.567	.409	.359	.889

Item-Total Statistics Factor 2

	Scale Mean if Item Deleted	Scale Variance if Item Deleted	Corrected Item-Total Correlation	Squared Multiple Correlation	Cronbach's Alpha if Item Deleted
It is difficult to package or stock the various forms of naloxone	25.34	40.039	.547	.471	.775
Naloxone expiration dates are too short	24.98	47.095	.468	.304	.789

The cost of stocking naloxone is too high	24.81	39.869	.634	.548	.757
It is difficult to obtain reimbursement from third-party payers	24.84	38.801	.715	.655	.741
The amount patients have to pay for naloxone is too high	24.44	42.663	.528	.551	.777
There is not enough profit margin	24.63	42.683	.647	.432	.759
Patients are not interested in receiving naloxone from the pharmacy	24.30	47.895	.257	.185	.825

Appendix K

Aim 2 Reliability Analysis: Motivation Scales

Social Gains

Item-Total Statistics

	Scale Mean if Item Deleted	Scale Variance if Item Deleted	Corrected Item-Total Correlation	Cronbach's Alpha if Item Deleted
On a scale of 1 to 7, please rate the extent to which you agree or disagree with the following statements regarding your MOTIVATION TO PARTICIPATE in naloxone services or training at your pharmacy, with 1 being strongly disagree and 7 being strongly agree. Factors motivating my participation in naloxone services or training include: - Being perceived as a pharmacy leader	23.98	10.016	.616	.746
Advancing the profession of pharmacy	23.48	11.762	.696	.711
Improving the image of my pharmacy in the community	23.98	11.131	.539	.769
Fulfilling my duty and obligation as a pharmacist to help patients	23.08	14.305	.499	.776
Improving the health and well-being of my patients	23.15	13.798	.649	.747

Social Losses

<div align="center">Item-Total Statistics</div>

	Scale Mean if Item Deleted	Scale Variance if Item Deleted	Corrected Item-Total Correlation	Cronbach's Alpha if Item Deleted
Preventing possible opioid overdose deaths in my community	13.58	14.739	.185	.664
Avoiding losing the status and respect of my professional peers	16.29	8.045	.530	.435
Avoiding being perceived as an uncompassionate and uncaring organization	15.90	6.515	.691	.254
Avoiding harm to my patients	13.98	12.967	.255	.637

Economic Losses

<div align="center">Item-Total Statistics</div>

	Scale Mean if Item Deleted	Scale Variance if Item Deleted	Corrected Item-Total Correlation	Cronbach's Alpha if Item Deleted
Complying with a professional manager or decision-maker's request	12.71	18.341	.148	.733
Avoiding potential loss of patients to pharmacy competitors	13.68	14.288	.537	.429
Avoiding future economic repercussions related to patient overdose	13.27	12.497	.628	.336
Preventing healthcare expenditures related to overdose treatment in my community	12.06	18.815	.341	.582

Economic Losses after Removing One Item

Item-Total Statistics

	Scale Mean if Item Deleted	Scale Variance if Item Deleted	Corrected Item-Total Correlation	Cronbach's Alpha if Item Deleted
Avoiding potential loss of patients to pharmacy competitors	9.15	8.421	.610	.579
Avoiding future economic repercussions related to patient overdose	8.74	7.145	.691	.466
Preventing healthcare expenditures related to overdose treatment in my community	7.53	12.155	.408	.799

Economic Gains

Item-Total Statistics

	Scale Mean if Item Deleted	Scale Variance if Item Deleted	Corrected Item-Total Correlation	Cronbach's Alpha if Item Deleted
Providing an additional revenue stream for my pharmacy	13.90	15.400	.765	.720
Providing a competitive advantage over other pharmacies	13.77	14.243	.830	.683
Saving staff time contacting physicians or other providers to prescribe naloxone	14.31	16.806	.696	.756
Improving the technical expertise and job skills of myself / my pharmacy staff	12.74	23.736	.335	.890

Technical Efficacy

Item-Total Statistics

	Scale Mean if Item Deleted	Scale Variance if Item Deleted	Corrected Item-Total Correlation	Cronbach's Alpha if Item Deleted
Providing an additional revenue stream for my pharmacy	26.61	58.405	.683	.843
Providing a competitive advantage over other pharmacies	26.48	54.877	.796	.825
Saving staff time contacting physicians or other providers to prescribe naloxone	27.02	58.114	.746	.834
Improving the technical expertise and job skills of myself / my pharmacy staff	25.45	70.055	.415	.874
Avoiding potential loss of patients to pharmacy competitors	27.39	56.995	.720	.837
Avoiding future economic repercussions related to patient overdose	26.98	56.278	.684	.843
Preventing healthcare expenditures related to overdose treatment in my community	25.77	68.112	.430	.873

Social Legitimacy

Item-Total Statistics

	Scale Mean if Item Deleted	Scale Variance if Item Deleted	Corrected Item-Total Correlation	Cronbach's Alpha if Item Deleted
Being perceived as a pharmacy leader	43.90	36.351	.436	.723

	Scale Mean if Item Deleted	Scale Variance if Item Deleted	Corrected Item-Total Correlation	Cronbach's Alpha if Item Deleted
Advancing the profession of pharmacy	43.40	37.556	.584	.704
Improving the image of my pharmacy in the community	43.90	35.695	.529	.706
Fulfilling my duty and obligation as a pharmacist to help patients	43.00	40.459	.507	.722
Improving the health and well-being of my patients	43.06	41.111	.483	.726
Preventing possible opioid overdose deaths in my community	43.00	41.115	.428	.729
Avoiding losing the status and respect of my professional peers	45.71	37.193	.278	.763
Avoiding being perceived as an uncompassionate and uncaring organization	45.32	33.107	.456	.726
Avoiding harm to my patients	43.40	38.441	.437	.723

Opportunity Framing

Item-Total Statistics

	Scale Mean if Item Deleted	Scale Variance if Item Deleted	Corrected Item-Total Correlation	Cronbach's Alpha if Item Deleted
Providing an additional revenue stream for my pharmacy	43.32	36.616	.459	.685
Providing a competitive advantage over other pharmacies	43.19	34.683	.530	.668
Saving staff time contacting physicians or other providers to prescribe naloxone	43.73	36.792	.491	.677

	Scale Mean if Item Deleted	Scale Variance if Item Deleted	Corrected Item-Total Correlation	Cronbach's Alpha if Item Deleted
Improving the technical expertise and job skills of myself / my pharmacy staff	42.16	41.416	.421	.693
Being perceived as a pharmacy leader	42.23	41.915	.294	.716
Advancing the profession of pharmacy	41.73	43.383	.372	.702
Improving the image of my pharmacy in the community	42.23	38.571	.538	.670
Fulfilling my duty and obligation as a pharmacist to help patients	41.32	47.402	.156	.727
Improving the health and well-being of my patients	41.39	46.208	.292	.714

Threat Framing

Item-Total Statistics

	Scale Mean if Item Deleted	Scale Variance if Item Deleted	Corrected Item-Total Correlation	Cronbach's Alpha if Item Deleted
Preventing possible opioid overdose deaths in my community	26.29	46.603	.039	.747
Avoiding losing the status and respect of my professional peers	29.00	32.066	.615	.635
Avoiding being perceived as an uncompassionate and uncaring organization	28.61	30.864	.642	.625
Avoiding harm to my patients	26.69	44.413	.117	.745
Avoiding potential loss of patients to pharmacy competitors	29.06	32.684	.555	.652

Avoiding future economic repercussions related to patient overdose	28.66	32.785	.490	.672
Preventing healthcare expenditures related to overdose treatment in my community	27.45	37.793	.445	.685