Program evaluation of academic detailing on naloxone prescriptions prescribed at the U.S. Department of Veterans Affairs

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A dissertation

submitted in partial fulfillment of the

requirements for the degree of

Doctor of Philosophy

University of Washington

2018

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Abstract

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Background

The rising incident of opioid overdose mortality has become a national epidemic in the U.S., especially among veterans whose mortality risk is twice that of the general population. The U.S. Department of Veterans Affairs (VA) implemented the Opioid Overdose Education and Naloxone Distribution (OEND) Program to provide education and training to providers and patients on opioid overdose prevention, recognition, response, and proper use of naloxone to reverse opioid-related overdose events. Penetration into the provider section required a partnership with the VA Pharmacy Benefits Management National Academic Detailing Service that delivers educational outreach to providers to align their naloxone prescribing to veterans at risk of an opioid overdose with evidence-based practice. This study focused on the impact of academic detailing on naloxone prescribing by evaluating the impact of the intervention as well as providers' perception of the program and naloxone use to reverse opioid overdose events. In

Aim 1, I evaluated the implementation strength of academic detailing at the VA from October 2014 to December 2017. This was complemented by Aim 2, which explored the providers' perception of academic detailing and captured facilitators and barriers to naloxone prescribing.

Methods

In Aim 1, a repeated measures, retrospective cohort design with a fixed effects negative binomial model was used to evaluate the impact of implementation strength (proportion of providers exposed to exposed to academic detailing) on total number of naloxone prescriptions prescribed for each VA station from October 2014 to December 2017. Setting was in the VA system, which consists of 130 stations comprised of VA Medical Centers and their surrounding clinics. I evaluated a closed cohort of primary care providers who wrote a prescription for an opioid.

In Aim 2, a mixed methods design was used to explore providers' perception of academic detailing and naloxone prescribing using a survey and identify barriers and facilitators using semi-structured phone interviews. Online survey was developed based on a conceptual framework using existing theories (Theory of Planned Behavior, Social Marketing Theory, and the Framework for effective implementation), tested for face validity, and deployed to providers using who recently received an OEND-specific academic detailing visit within 2 to 4 weeks across the VA. Semi-structured phone interviews were conducted with providers who finished the survey and agreed to continue their participation.

Results

In Aim 1, there was a total of 5,452 providers who wrote for an opioid prescription. Increasing the proportion of providers exposed to academic detailing at each VA station from 0% to 100% was associated with a of 5.51 times higher incidence (95% CI: 1.86, 16.27) in the monthly number of naloxone prescriptions prescribed. Alternatively, this was a 9.13 increase in the monthly number of naloxone prescriptions.

In Aim 2, 137 (12.2%) providers completed the survey. The average domain score for responders was highest for Satisfaction (6.28) followed by Attitude (6.02), Knowledge (5.96), Social norms (5.64), and Perceived barriers (4.86). Knowledge, Social norms, and Satisfaction domains were similar across the different provider types. However, pain specialists had a higher Attitude score (+0.56, P=0.011) and Perceived barriers score (+0.82, P=0.009) than primary care providers. A total of 11 responders participated in phone interviews. Participants identified limited time, poor data integration, social stigma, and lack of homeless support as barriers to prescribing naloxone. A patient list generated by academic detailers was identified as a facilitator to prescribing naloxone.

Conclusions

By combining the findings from these different approaches, I was able to develop a deeper understanding of academic detailing's effectiveness to increase naloxone prescriptions prescribed as its phenomena for augmenting providers' naloxone prescribing behavior.

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Acknowledgements

In the five years that I have spent at the University of Washington (UW), I was fortunate enough to have mentors, instructors, and classmates who guided, illuminated, and inspired me. They taught me that socializing, watching movies, and playing video games were actually normal activities and not considered atypical for a struggling and impoverished graduate student. For those lessons, I am forever grateful. Additionally, my family and friends have shown great patience and empathy towards me during my early days in the program. Without their love, humor, and simple life lessons, I would have been too stressed to enjoy this entire experience. Moreover, this work wouldn't have been possible without the support of the Elmer M. Plein Research Endowment Fund, Agency for Healthcare Research and Quality (grant number T32HS013853), and the U.S. Department of Veterans Affairs Pharmacy Benefits Management Academic Detailing Service. (The content is solely the responsibility of the authors and does not necessarily represent the official views of the Agency for Healthcare Research and Quality or the U.S. Department of Veterans Affairs.) Finally, I want to thank my committee members and chair for their time in reading this tome, taking the risk for accepting me into the program, and making sure that I graduate before the 10-year limit.

Dedication

This work is dedicated to the veterans, active duty personnel, and their family and friends of the United States of America. Without their commitment, sacrifice, and sense of duty, we would not be able to enjoy the liberty and freedom we possess and the promise of a better existence.

Chapter 1: Introduction

Background

Opioid overdose is a major epidemic in the U.S. with an incidence rate of 14.7 events per 100,000 persons in 2014.[1] Among the general population, opioid overdose has surpassed motor vehicle mortality in the by 150% in 2014.[1] The Centers for Disease Control and Prevention (CDC) reported that opioid overdose mortality has increased by 200% in the last decade.[1] Further, the mortality rate was twice as high among Veterans compared to the general population in 2005 [standardized mortality ratio=1.96 (95% CI: 1.83, 2.08)].[2] Between 2001 and 2007, opioid prescribing in Veterans increased by 184% for methadone, 60% for synthetic/semi-synthetic opioids, and 35% for non-synthetic opioids, which has been associated with increased opioid overdose mortality.[3] Naloxone, an opioid overdose reversal agent, has been identified as a crucial element in the overall strategy to prevent opioid overdose mortality; however, reluctance by providers to prescribe naloxone limits its effectiveness in preventing opioid overdose mortality.[4,5] Although naloxone distribution programs are in place across the U.S., they do not sufficiently address the risk in Veterans.[6]

Opioid overdose is caused by respiratory depression induced by opioid binding to μ-receptors in the brain. This process is reversed with naloxone, an opioid antagonist that was approved by the Food and Drug Administration (FDA) to reverse the effects of opioid overdose and restore respiratory function. In some states, naloxone does not require a prescription, and can be delivered intravenously, intramuscularly, and intranasally. Naloxone has been reported to decrease opioid overdose mortality if used correctly and has a survival rate ranging from 83% to 100%.[6] Community-based opioid overdose prevention programs have been created to provide

access to naloxone in response to the growing epidemic. In San Francisco, the Drug Overdose Prevention and Education (DOPE) Project reported that program participants reversed 89% of 399 overdose events using naloxone from 2003 to 2009.[7] In Massachusetts, the naloxone kit community distribution program reduced opioid overdose mortality from 46% to 22% between 2002 and 2009.[8] In Chicago, a comprehensive program targeting heroin users that included naloxone-use training decreased opioid overdose mortality by 20% in 2001 and, subsequently, by 10% in 2002 and 2003.[9] Despite its efficacy and safety profile, naloxone is underutilized at the VA. Until 2014, an outpatient prescription for naloxone was not orderable at the VA.[10] This has been attributed to several reasons, as described below.

Critical barriers

Prescribers are reluctant to prescribe naloxone to patients who are at-risk of opioid overdose mortality. In several focus group interviews, clinical staff from a large health care system, managed care organization, and an academic medical center articulated several reasons for not prescribing naloxone as a reversal agent for opioid overdose mortality.[5] Participants feared that prescribing naloxone would result in moral hazard - a situation where opioid users develop riskier behavior owing to the fact that naloxone provides insurance for an overdose. Additionally, prescribers were worried about offending patients by 'cherry-pick[ing]' them from other patients, highlighting the patient's fear of being identified as an illicit-drug user. Moreover, prescribers also reasoned that they were only treating the symptoms rather than the underlying problem of opioid overdose. Matheson and colleagues[11] reported that providers felt insufficiently knowledgeable and skilled to prescribe naloxone. Consequently, providers considered that naloxone prescribing should be reserved for specialists trained in addiction or pain management.

Proper education using innovative evidence-based approaches, such as academic detailing, can dispel these fears and promote an effective and safe naloxone prescribing practice that will reduce opioid overdose mortality.

Academic detailing

Academic detailing is best described as a "service that provides interactive educational outreach utilizing social marketing to engage the prescriber and meet his or her specific educational needs."[12] The term "academic detailing" was first coined by Jerry Avorn and Stephen B. Soumerai in their 1983 seminal paper;[13] the former whom described academic detailing as an "educational outreach program[s] in which independent researchers and clinicians systematically review data for a given therapeutic area and develop noncommercial, evidence-based recommendations about treatment choices."[14] Using social marketing methods to target and educate prescribers, academic detailers introduce evidence-based research to support best prescribing practices by educating prescribers using "key messages." The basic principles of academic detailing incorporate relationship building, comparative effectiveness evidence, cost-effectiveness evidence, and guidance using "key message"-focused discussions with prescribers. The "key messages" (factors and methods) specifically for naloxone include proper use of the drug, identification of eligible patients, and focus on the overall goal of preventing opioid overdose mortality. A list of these "key messages" are summarized in **Table 1.1.**

Academic detailing has been successful in changing prescriber behavior to be aligned with best-practice guidelines in a variety of clinical settings. Academic detailing has been responsible for improved colorectal cancer screening,[15] judicious use of antibiotics,[16] appropriate treatment for

alcohol use disorder,[17] and improved adherence to antihypertensive guidelines.[18] However, there is a paucity of data on the impact of academic detailing on naloxone or opioid use. A search of the literature yielded an ongoing randomized trial designed to evaluate a multicomponent strategy to improve opioid therapy guidelines to reduce opioid misuse has begun enrolling patients.[19] This multicomponent strategy involves nurse care management, use of a patient registry, academic detailing, and electronic tools. Despite past evidence of successes in other clinical areas, our knowledge of academic detailing in preventing and reducing opioid death is limited. Moreover, very little is known about the prescriber and academic detailer's perception of the facilitators and barriers to adoption of "key messages" delivered by the academic detailer, and whether this education is synthesized by prescribers into the desired prescribing behavior.

The U.S. Department of Veterans Affairs (VA) Mental Health Initiative (MHI) is a broad-spectrum operation to develop and initiate programs, hire and retain staff, and promote the well-being of veterans with mental health illness such as depression, post-traumatic stress disorder, schizophrenic disorders, insomnia, and alcohol/substance abuse use disorder. The VA National Academic Detailing Service, an element of the MHI, was initially piloted at VA facilities in California, Nevada, and the Pacific Islands (labeled as Veterans Integrated Service Networks 21 and 22) in 2010. The overarching goal of the Academic Detailing Service is to educate prescribers through interactions with academic detailers using evidence-based research, data tools, and benchmarking in order to change prescribing behavior and improve adherence to evidence-based practices. These educational outreach visits can result in improved efficacy, safety, and cost-effectiveness.[12,13,20–22]

To address the rising opioid overdose mortality in Veterans, the VA implemented the Opioid Overdose Education and Naloxone Distribution (OEND) program, which collaborated with the VA Academic Detailing Service to implement academic detailing as an innovative solution.[23] As a result, the VA Academic Detailing Service targeted providers with at-risk populations for opioid overdose mortality to deliver OEND-specific educational outreach, in particular, "key messages" to naloxone treatment guidelines with the goal of increasing access to naloxone prescriptions to reduce or prevent opioid overdose mortality.

Rationale

Despite a large body of evidence supporting academic detailing in aligning prescribing behavior with evidence-based practice, very little is known about its impact on mental health at the national level in the VA. In theory, it is believed that providers, after their interaction with an academic detailer, will increase their naloxone prescriptions prescribing to reverse opioid overdose events. A recent study reported that VA providers who were exposed to academic detailing had a greater rate of naloxone prescriptions prescribed compared to providers who didn't across 24 months.[24] However, the authors noted that national implementation of academic detailing across the VA was not uniform and prone to budget constraints, which may have hinders delivery of these critical OEND-specific educational outreach visits. Therefore, it was necessary to evaluate the impact of academic detailing implementation on naloxone prescriptions prescribed so that decision- and policy-makers can develop strategies to provide quality and optimal care to their veterans.

Implementation process can be measured based on its quality, strength, and fidelity.[25–28] However, generating data on these implementation elements is challenging and difficult. Fortunately, we were able to capture the quantity of the intervention (number of provider exposed to OEND-specific academic detailing), which became a proxy for implementation strength. In Aim 1 of this study, implementation strength was used to evaluation the impact of implementation on naloxone prescribing trends across the VA from October 2014 to December 2017.

Our understanding of academic detailing's phenomena is limited. We have come to understand that academic detailing used elements of the social marketing framework[29] to augment providers' prescribing behavior. But this complex process also requires incorporation other theoretical frameworks, such as the Theory of Planned Behavior[30] and the Framework for Effective Implementation,[25] to completely understand why and how academic detailing works. It was necessary to explore the different themes associated with provider prescribing changes so that program managers can develop action plans to optimize academic detailing's delivery of key messages and increase the chance for providers to adopt these messages to align their prescribing practice with evidence-based practice. Therefore, in Aim 2, a mixed method study was used to explore providers' perceptions of academic detailing and naloxone prescribing for opioid overdose reversals in the outpatient setting and identify facilitators and barriers to providing naloxone to patients at risk for opioid overdose.

Innovation

Most program evaluations only include the quantitative analysis, which are derived from administrative records and evaluate the association between academic detailing and prescribing changes. This study is innovative because it will examine the implementation evaluation results with data from a mixed methods study (combination of an online survey and semi-structured interviews) that aim to identify perceived barriers and facilitators for implementing a successful academic detailing program and to further explore the relationship between academic detailing and naloxone prescribing patterns. Altogether, these findings will deepen our understanding of "how" academic detailing works and inform decision makers and program managers to develop strategies to improve and optimize academic detailing.

Tables and Figures

Table 1.1. Features and methods ("key messages") associated with OEND-specific educational outreach delivered by the academic detailer.

Elements denoted as "key messages"	
Appropriate documentation (OEND)	Naloxone Kit Instructions--Autoinjector
OEND Policy Education	Naloxone Kit Instructions--Intramuscular
OEND Implementation Strategy/Logistics	Naloxone Kit Instructions--Intranasal
Candidates for Naloxone Kits	Opioid Safety for Patients on Opioids
Utilization of Naloxone Kit	Opioid Safety for Patients with SUD
Reporting Naloxone Refills/Reversals	Opioid Safety Naloxone Kit Brochure
OEND Dashboard	Overdose Toolkit
High Risk Patients (OEND)	OEND Quick Reference Guide

OEND, Opioid Overdose Education and Naloxone Distribution

SUD, Substance-Use Disorder

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Chapter 2: National implementation of academic detailing service on naloxone prescribing trends at the United States Department of Veterans Affairs: A retrospective cohort study

Abstract

Objective

Academic detailing in partnership with the Opioid Overdose Education and Naloxone Distribution Program was implemented to increase access to naloxone to prevent opioid overdose mortality in veterans at U.S. Department of Veterans Affairs (VA). However, implementation was not uniform leading to varying levels of academic detailing exposure which may impact naloxone prescribing. We examined the impact of implementation strength defined as proportion of providers exposed to academic detailing at each station on naloxone prescribing from September 2014 to December 2017.

Data sources

We used the VA Corporate Data Warehouse for data on pharmacy dispensing, station-, provider- and patient-level characteristics. Academic detailing activities came from data recorded by academic detailers using Salesforce.com.

Study design and setting

We used a repeated measures, retrospective cohort design with a fixed effects negative binomial model. Setting was in the VA system, which consists of 130 stations comprised of VA Medical Centers and their surrounding clinics.

Principal findings

Increasing the proportion of providers exposed to academic detailing from 0% to 100% was associated with a 9.13 increase in the monthly number of naloxone prescriptions.

Conclusions

Our findings highlight the importance of implementation process for academic detailing. Decision makers must carefully consider the implementation process to achieve the greatest effectiveness from the intervention.

Background

Opioid overdose deaths have become a national epidemic and public health policy concern in the United States (U.S.). The number of opioid-related overdose death in the U.S. has increased by 28% between 2015 and 2016.[1] Compared to the general U.S. population, mortality risk is two times higher among veterans.[2] This had been exacerbated by the increased use of opioids in veterans. Between 2001 and 2007, opioid prescribing in veterans increased by 184% for methadone, 60% for synthetic/semi-synthetic opioids, and 35% for non-synthetic opioids[3] In response to the opioid crisis, the U.S. Department of Veterans Affairs (VA) implemented system-wide programs such as the Opioid Safety Initiative (OSI) in 2013[4] and Opioid Overdose Education and Naloxone Distribution (OEND) program in 2014[5] While the goal of OSI is to promote the proper and safe prescribing of opioids for pain management;[4,6] the OEND program is focused on educating patients, their caregivers, and providers on opioid overdose prevention, recognition, response, and proper use of naloxone to reverse opioid-related overdose events.[5]

Naloxone is an effective and safe strategy for preventing opioid overdose mortality.[7] However, lack of knowledge and stigma associated with opioid use disorder has contributed to the reluctance by providers to prescribe naloxone, limited its use in the ambulatory setting, and thereby its effectiveness in preventing opioid overdose mortality.[8–10] In order to change provider prescribing behavior, specifically for veterans, and improve access to naloxone for opioid reversals, the OEND program collaborated with the VA Pharmacy Benefits Management Academic Detailing Service to implement academic detailing as an innovative solution to educate and inform providers on the proper use of naloxone.

Academic detailing is a multifaceted, educational outreach intervention that educates prescribers through interactions with academic detailers (specially trained clinical pharmacists) using evidence-based research, educational brochures, and benchmarking tools in order to align prescribing behavior with best practices also denoted as "key messages" in the literature.[11–15] Academic detailing has been associated with improved adherence to treatment guidelines in other diseases (e.g., hypertension,[16] alcohol-use disorder,[17] colorectal cancer screening,[18] and judicious use of antibiotics[19]). In the VA, academic detailers identify prescribers using priority panels of high-risk patients, arrange one or more visits with prescribers, and share naloxone-prescribing data along with population management tools that highlight veterans at risk for opioid overdose events, with the goal of improving adherence to evidence-based practices and access to naloxone treatment.

On March 27th 2015, the Interim Under Secretary of Health mandated that all VA networks implement academic detailing to address issues related to pain management and mental health by June 30th 2015.[20] Since the mandate was announced, VA networks slowly implemented academic detailing generating a variety of start dates that was conditioned on the funding allocated and other competing priorities at each station. Consequently, implementation varied across all the VA stations, which may affect academic detailing's impact on naloxone distribution.

We were concerned that different levels of academic detailing implementation would impact the degree of naloxone prescriptions prescribed. By measuring the proportion of providers exposed to OEND-specific academic detailing as a proxy for implementation strength (quantity of the

intervention delivered),[21] we can assess the scale up of academic detailing and guide efforts to improve academic detailing's effectiveness. An increase in implementation strength will result in higher fidelity and therefore, increases in naloxone prescriptions prescribed. Furthermore, we hypothesized that stations that implemented academic detailing will have a greater number of naloxone prescriptions prescribed than stations that did not implement academic detailing.

The objective of this study was to examine the impact of station-level implementation strength of academic detailing across the VA on naloxone prescribing from September 2014 to December 2017.

Methods

This was a repeated measures, retrospective cohort study that investigated the association between implementation strength (proportion of providers exposed to OEND-specific academic detailing) and total count of naloxone prescriptions prescribed from September 2014 to December 2017. The study protocol was reviewed and approved by Institutional Review Boards at the Veterans Affairs San Diego Healthcare System (#H160146) and University of Washington (#52272).

Sample

This study was performed at the U.S. Department of Veterans Affairs, which is the largest, integrated healthcare system in the U.S. with coverage to all fifty states and its territories and a total enrollment of approximately 9 million veterans.[22] In 2017, the VA was comprised of 130 stations (or regional facilities), which encompass 179 Veterans Affairs Medical Centers (VAMCs) and 1,061 Community-Based Outpatient Clinics (CBOCs) that performed

approximately 109 million outpatient visits, treated 615 thousand inpatients (medical and surgical), and treated 149 thousand mental health inpatients.[23] The VA has a total workforce of approximately 25 thousand physicians and 95 thousand nurses with an annual operating budget of approximately $72 billion.

This analysis was performed at the station level; all stations (N=130) across the VA were included. Each station consists of one or more VAMCs with its surrounding satellites or CBOCs. Providers are assigned to a station but may work at either the VAMC, CBOC, or both.

We used provider-level data to generate station-level characteristics (e.g., mean age of providers; proportion of providers who are male, physician assistants, nurse practitioners, and mental health specialists). A closed cohort of providers who had uninterrupted employment at the Veterans Health Administration from September 2014 to December 2017 was selected. Providers were included if they prescribed at least one opioid prescription and had patients in their care who were at risk for opioid-related events (e.g., overdose and mortality). Providers were excluded if they were pharmacists, residents, anesthesiologists, surgeons, oncologists, or worked in the emergency department. The focus was on providers who provided care for a group of patients on a continual basis. Therefore, we restricted our provider sample to primary care. All providers had patients assigned throughout the study period.

Patients were included if they had at least one opioid prescription. High risk patients were defined as any patient with an opioid prescription with at least one of the following: an opioid use disorder (OUD) abuse and dependence diagnosis, at least one methadone prescription, a

daily dose of 50 morphine equivalents or greater (50 MEDD), and Risk Index for Overdose or Serious Opioid-induced Respiratory Depression (RIOSORD) class >/= 5. The RIOSORD is a risk tool used by the VA to identify patients at risk for respiratory depression due to opioid overdose; a class of 5 or greater is associated with a risk of 46%.[24] A list of diagnosis codes used to identify patients for each provider is presented in **Appendix A.2.1**. Patient assignment to providers was based the Patient Centered Management Module (PCMM), an enterprise application that assigns patients to health care teams that delivers comprehensive care.[25]

Data source

Station-, provider-, and patient-level data were accessible using the VA Corporate Data Warehouse (CDW), which is the central repository for pharmacy, outpatient, inpatient, and staff data.[26] Data on provider exposure to academic detailing were obtained from Salesforce.com® (San Francisco, CA), an online cloud-based platform designed for customer relationship management, data collection, and reporting. Academic detailers recorded their educational outreach activities with providers capturing the date the visit occurred, topics discussed during the visit, educational materials and data tools used during the visit, and duration of the visit.

Dependent variable

The evaluated outcome was the total count of naloxone prescriptions prescribed, compiled from CDW pharmacy claims data by month and aggregated by station. We did not include formulations of naloxone that contained buprenorphine (Suboxone®) due to its specific indication for opioid use disorder, which excludes its utility in opioid-related emergencies. Prior to the FDA-approval of commercial forms of outpatient naloxone autoinjector (Evzio® 2014) and nasal spray (Narcan® 2016), the VA dispensed naloxone vials accompanied by a syringe or

nasal atomizer. Hence, we included all formulations of naloxone in our total count. Prior to 2014, the VA did not have naloxone as an orderable medication; hence, the first naloxone prescriptions for outpatient use to reverse opioid overdose were prescribed in October 2014.

Predictor of interest

Academic detailing's implementation strength was measured as the proportion of providers who received OEND-specific academic detailing at each station per month between September 2014 to December 2017. We fixed the provider population at each station by using a closed cohort to generate consistent values of the proportion of providers who received OEND-specific academic detailing. Therefore, newly hired providers could not enter the cohort and providers could not leave the cohort during the study period. The proportion of providers exposed to academic detailing represented the time-varying measurement of academic detailing implementation strength at each station across time. Providers were categorized as exposed to academic detailing when they received their first educational OEND-specific outreach visit specific with an academic detailer.

Independent variables

We controlled for time-varying covariates at the station level by month in our regression models, which included the number of outpatient visits, number of emergency department and urgent care visits, number of inpatient admissions, and number of prescriptions released.

Analytic strategy

Descriptive analysis was performed on baseline characteristics of the station and provider cohort. Continuous data was presented as mean with standard deviation and discrete data was presented

as frequency with percentages. One-way analysis of variance was performed to compare the mean station-level baseline characteristics across different proportion of providers exposed to academic detailing categorized as 0%, >0% to 25%, >25% to 50%, >50% to 75%, and >75% to 100% of providers exposed to the intervention at the end of the study period).

In the primary analysis, we investigated the association between the proportion of providers exposed to academic detailing and the total number of naloxone prescriptions prescribed in a veteran population who received an opioid prescription (Model 1). In our secondary aims, we further explored this relationship on specific patient subgroups in addition to those patients who received an opioid prescription. These subgroups included patients categorized as high risk (Model 2), prescribed 50 MEDD or greater (Model 3), had a RIOSORD class of 5 or greater (Model 4), were diagnosed with an opioid use disorder or related substance abuse disorders (Model 5), and prescribed methadone (Model 6), (**Appendix A.2.1** contains the ICD 9 and ICD 10 diagnostic codes for each subgroup).

Results from the count models were presented as the expected log count of naloxone prescriptions prescribed with corresponding 95% confidence intervals (CI). We also reported the outcome in terms of incident rate ratio (IRR) with 95% CI.

Since the dependent variable was the total count of naloxone prescriptions prescribed, a non-linear model was selected to address the main objective of this study. To identify the correct functional form, we initially used a Poisson model, but the test for overdispersion to assess the mean-variance relationship did not hold. As a result, we used a negative binomial model which

incorporates an overdispersion parameter λ_i, is assumed to be constant at each station and is expressed as

$$\Pr(Y = y_{it}|\mu_{it}, \lambda_i) = [\Gamma(y_{it} + \lambda_i)/(\Gamma(y_{it} + 1) * \Gamma(\lambda_i))] * (\mu_{it}/\mu_{it} + \lambda_i)^{y_{it}} * (\lambda_i/\lambda_i + \mu_{it})^{\lambda_i},$$

with mean and variance functions

$$E(y_{it}) = \mu_{it}$$

$$var(y_{it}) = \mu_{it}(1 + \mu_{it}/\lambda_i)$$

In a panel dataset using a negative binomial regression model, the total number of naloxone prescriptions prescribed for station *i* at time *t* is denoted by μ_{it} and follows the exponential expression

$$\mu_{it} = \exp\left(\ln(t_{it}) + \beta_0 + \beta_1 prop_{it} + \beta_2 month_{it} + \beta_j \boldsymbol{time_i} + \beta_k \boldsymbol{station_i} + \beta_l \boldsymbol{X_{lit}}\right)$$

where $prop_{it}$ denotes the main predictor of interest (proportion of providers exposed to OEND-specific academic detailing, for station *i* at time *t*), $month_{it}$ denotes the month for station *i* at time *t*, $\boldsymbol{time_i}$ denotes the time-fixed effects for each station *i*, $\boldsymbol{station_i}$ denotes the station-fixed effects for each station *i*, $\boldsymbol{X_{lit}}$ is a vector that denotes each time-varying covariate *l* for station *i* at time *t*, and $\ln(t_{it})$ denotes the number of eligible patients who should receive naloxone for station *i* at time *t* (offset term). The offset term is time-varying and adjusted for the opportunities patients has to being prescribed naloxone at each month. The intercept is denoted by β_0 and the β coefficients represents the expected log odds count of naloxone.

Fixed effects regression model is advantageous in reducing bias associated with unobserved station-level time-invariant covariates; otherwise known as omitted variable bias.[27,28] Moreover, fixed effects regression model allows for the *i*-th subject (e.g., station) to act as their own control as repeated measures of the outcome (total count of naloxone prescriptions prescribed) are made

across time yielding the within effects estimator. If assumptions hold, then the fixed effects model can generate causal interpretation of the change in proportion of providers exposed to academic detailing with the change in the total count of naloxone prescriptions prescribed.

With the fixed effects negative binomial model, the conditional maximum likelihood estimation does not yield true fixed effects results. In 1984, Hausman, Hall and Griliches provided an approach to estimate the conditional maximum likelihood method for the fixed effects negative binomial regression (denoted as the HHG model).[29] However, in 2002, Allison and Waterman reported that the HHG model is not a true fixed effects model because it allows for subject-level variation in the overdispersion parameter λ_i instead of the conditional mean, which would result in non-zero coefficients for time-invariant covariates.[28] Other researchers also demonstrated this limitation of the HHG model.[30,31] In order to address this issue, Allison and Waterman proposed using an unconditional maximum likelihood estimation fixed effects negative binomial regression by including dummy variables for all panel-level subjects.[28] Based on the recommendation by Allison and Waterman, we used the unconditional maximum likelihood estimation of the fixed effects negative binomial regression to estimate the impact of the proportion of providers exposed to academic detailing on the monthly total naloxone prescriptions prescribed. Model fit was determined using the Akaike Information Criterion (AIC) and Bayesian Information Criterion (BIC) in addition to the Hosmer-Lemeshow test.

We estimated the mean total number of naloxone prescriptions prescribed by taking the numerical derivative of the expected total monthly naloxone prescriptions prescribed with respect to the proportion of each station:

$$\partial E[Y|\boldsymbol{X}]/\partial prop = e^{\boldsymbol{\beta X}} * \beta_1$$

where $\boldsymbol{\beta X}$ denotes the average marginal effect and β_1 represents the coefficient for the proportion of providers exposed to academic detailing. We also measured the marginal effect at different levels of the proportion at 0%, 25%, 50%, 75%, and 100%.

All analyses were performed using Stata 15.0 SE (Stata Corp, College Station, TX).

Results

Our analysis included 130 stations with 40 months of follow-up for a maximum total of 5200 panel-level observations. We used data that included a total of 5,425 providers (**Table 2.1**) spread across 130 stations. Providers were on average 54.4 (9.5) years old (age data were missing for 935 providers); the majority were female (56%). All providers were in primary care and composed of physicians (72%), nurses (22%), and physician assistants (6%). A small proportion of primary care providers were also categorized as mental health providers (1%). Station-level characteristics are summarized in **Table 2.2**. At the station-level, there were, on average, 83,280 (SD 51,184) outpatient visits per month, 1,714 (SD 1,124) emergency department and urgent care visits per month, 492 (SD 384) inpatient admissions per month, and 93,592 (SD 54,618) prescriptions released per month. Moreover, baseline characteristics of stations were not significantly different across various quintiles of implementation strength (**Table 2.3**).

The implementation strength of academic detailing varied across stations as illustrated in **Figure 2.1**. The average proportion of providers exposed to academic detailing was 0.14 across the

study period with an overall standard deviation of 0.23 (within SD, 0.16, and between SD, 0.16). The minimum proportion of providers exposed to academic detailing was 0.00 and the highest was 0.94. Twenty-seven stations (21%) that did not have any exposure to academic detailing during the study time period. Overall, the average proportion of providers exposed to academic detailing increased across the study time period (**Figure 2.2**).

Figure 2.3 illustrates the trends associated with the average number of naloxone prescriptions prescribed, average proportion of patients who received naloxone, and the number of naloxone-eligible patients by different subgroups. Variations in the trends across different opioid overdose risk groups were apparent. In general, naloxone prescriptions prescribed and the proportion of naloxone-eligible patients who received naloxone increased as the number of patients eligible to receive naloxone decreased over time. The average number of naloxone prescriptions prescribed per month remained constant for the OUD, and methadone subgroups. Few changes were observed in the number of naloxone-eligible patients for the methadone subgroup.

Primary results

Patients prescribed an opioid prescription

Results of the count model regressions among patients with opioid prescriptions are presented in **Table 2.4**. There was a significant association between the proportion of providers exposed to academic detailing and the total count of naloxone prescriptions at each station per month. In Model 1, a one-unit increase (translated as a change from 0% to 100%) in the proportion of providers exposed to academic detailing was significantly associated with a 1.71 (95% CI: 0.62, 2.79) increase in the monthly expected log count of naloxone prescriptions prescribed at each station or a 5.51 times higher incidence (95% CI: 1.86, 16.27) in the monthly number of

naloxone prescriptions prescribed. Alternatively, we can interpret this as the marginal effect of increasing the proportion from 0% to 100% was a 9.13 increase in the number of naloxone prescriptions prescribed. We plotted the relationship between the marginal effect of the intervention at different levels of the proportion of providers exposed to OEND-specific academic detailing (**Appendix A.2.2**). As the proportion of providers exposed to academic detailing increase, the marginal effect of the intervention on the number of naloxone prescribed increased.

Exploratory subgroup analyses

Patients labelled as high risk

Model 2 evaluated a subgroup of patients who were categorized as high risk of having an opioid overdose. In Model 2, one-unit change in the proportion of providers exposed to academic detailing was significantly associated with a 1.55 (95% CI: 0.55, 2.56) increase in the monthly expected log count of naloxone prescriptions prescribed at each station or a 4.73 times higher incidence (95% CI: 1.73, 12.93) in the monthly number of naloxone prescriptions prescribed. Alternatively, we can interpret this as the marginal effect of increasing the proportion from 0% to 100% was a 5.26 increase in the number of naloxone prescriptions prescribed. Similar to the primary analysis, as proportion of providers exposed to academic detailing increase, the marginal effect of the intervention on the number of naloxone prescribed increased (**Appendix A.2.3**).

Patients with 50 MEDD or greater

Model 3 evaluated a subgroup of patients who were categorized having an MEDD of 50 or greater. In Model 3, one-unit change in the proportion of providers exposed to academic detailing was significantly associated with a 1.50 (95% CI: 0.46, 2.55) increase in the monthly

expected log count of naloxone prescriptions prescribed at each station or a 4.49 times higher incidence (95% CI: 1.58, 12.75) in the monthly number of naloxone prescriptions prescribed. Alternatively, we can interpret this as the marginal effect of increasing the proportion from 0% to 100% was a 3.75 increase in the number of naloxone prescriptions prescribed. There was a positive association between the marginal effect of the intervention with the different levels of exposure; however, the effect was not as steep as in the previous analyses (**Appendix A.2.4**)

Patients with a RIOSORD class of 5 or greater

Model 4 evaluated a subgroup of patients who were categorized having a RIOSORD class of 5 or greater. In Model 4, one-unit change in the proportion of providers exposed to academic detailing was significantly associated with a 1.44 (95% CI: 0.15, 2.73) increase in the monthly expected log count of naloxone prescriptions prescribed at each station or a 4.22 times higher incidence (95% CI: 1.16, 15.29) in the monthly number of naloxone prescriptions prescribed. Alternatively, we can interpret this as the marginal effect of increasing the proportion from 0% to 100% was a 4.26 increase in the number of naloxone prescriptions prescribed. The positive association between the marginal effect of the intervention with the different levels of exposure continued to be reported with the subgroup of patients with RIOSORD class of 5 or greater (**Appendix A.2.5**)

Patients with Opioid Use Disorder

Model 5 evaluated a subgroup of patients who were categorized having an OUD diagnosis. In Model 5, one-unit change in the proportion of providers exposed to academic detailing was nonsignificantly associated with a 0.85 (95% CI: -0.13, 1.83) increase in the monthly expected log count of naloxone prescriptions prescribed at each station or a 2.35 times higher incidence (95% CI: 0.88, 6.26) in the monthly number of naloxone prescriptions prescribed. Alternatively,

we can interpret this as the marginal effect of increasing the proportion from 0% to 100% was a 0.40 increase in the number of naloxone prescriptions prescribed. The positive association between the marginal effect of the intervention with the different levels of exposure continued to be reported with the subgroup of patients with OUD subgroup (**Appendix A.2.6**)

Patients with methadone

Model 6 evaluated a subgroup of patients who were categorized having a methadone prescription. In Model 6, one-unit change in the proportion of providers exposed to academic detailing was nonsignificantly associated with a 1.37 (95% CI: -0.08, 2.81) increase in the monthly expected log count of naloxone prescriptions prescribed at each station or a 3.93 times higher incidence (95% CI: 0.93, 16.66) in the monthly number of naloxone prescriptions prescribed. Alternatively, we can interpret this as the marginal effect of increasing the proportion from 0% to 100% was a 1.19 increase in the number of naloxone prescriptions prescribed. Although there continued to be a positive relationship between the marginal effect of the intervention and the different levels of exposure, this was mitigated in the methadone subgroup population (**Appendix A.2.7**).

Discussion

Due to the partnership between the VA OEND Program and the Academic Detailing Service, the VA dispensed over 100 thousand naloxone prescriptions to over 90 thousand veterans by the end of November 2017.[32] A previous study reported that providers exposed to OEND-specific academic detailing prescribed a greater number of naloxone prescriptions compared to providers who were not exposed; but did not account for the impact of implementation.[33] Our study takes this further by incorporating implementation strength across stations by evaluating the strength

(or intensity) of implementation in the form of the proportion of providers who received OEND-specific academic detailing. We reported that increasing the proportion of providers exposed to OEND-specific academic detailing from 0% to 100% was associated with a monthly marginal effect of 9.13 naloxone prescriptions prescribed at each station.

We can only hypothesize what type of implementation issues prevented a uniform and rapid diffusion of academic detailing across the VA stations. It is critical that further investigation include a qualitative analysis to identify themes and constructs associated with barriers to rapid diffusion of academic at VA stations with low proportion of providers exposed to the intervention. Rurality and distance from the VA Medical Centers or CBOCs are potential reasons that could limit provider exposure to academic detailing; and advances in telehealth may be potential solutions to increase penetration into these difficult areas. Currently, the VA is investigating the potential to provide educational outreach to providers using VA Video Connect systems.[34] However, it is unclear whether a virtual approach will alter the effect of a one-on-one encounter between a provider and an academic detailer. Non-verbal cues may not be captured with virtual systems and rapport could be adversely affected. Future analysis will need to address these issues to deepen our understanding about the implementation elements of academic detailing that are effective at promoting naloxone prescribing behavior changes.

During the study period the VA implemented other strategies to address the opioid epidemic such as the Opioid Safety Initiative to reduce opioid overuse. Recently, from mid-2012 to mid-2016, there was a 25% reduction in the number of opioids dispensed per quarter, a 47% reduction in the number of patients on concomitant benzodiazepine and opioid prescriptions, and

a 36% reduction in the number of patients receiving opioids doses of 100 MEDD or greater.[4] Therefore, it was necessary that we control for the time-varying effects of these changes in our fixed-effects model. While controlling for these time-varying covariates, we reported a significant increase in monthly total naloxone prescriptions prescribed at stations that implemented academic detailing.

On March 1st 2018, the White House Opioid Summit brought key leaders in healthcare together to discuss strategies that the federal government employs to address the opioid crisis. Dr. Shulkin, Secretary of the Department of Veterans Affairs, disclosed the S.T.O.P. P.A.I.N. initiative, which is a multifaceted approach to address the opioid crisis by using academic detailing alongside of other best practice strategies including the OEND Program to target providers and align them with evidence-based practice for pain management.[35] Among the goals of the Academic Detailing Service and the OEND Program is to perform educational outreach visits with providers who care for a patient population at risk of opioid-related overdose, with the goal of increasing their adherence to naloxone prescribing guidelines. The findings from this study support the policies that were recently enacted by the VA and provide empirical support that OEND-specific academic detailing on naloxone use increased prescriptions and can potentially reduce opioid overdose mortality.

Successful implementation involves many factors from fidelity to strength.[21,36] However, it is difficult to generate metrics of implementation that properly capture its impact on the program's outcome. We decided to use proportion of providers who received OEND-specific academic detailing to represent implementation strength because the academic detailers documented each

encounter on Salesforce®. We did not have data on implementation fidelity, quality, and adaptability. These factors are critical when assessing the program's impact on naloxone prescribing.[21] However, we took advantage of this natural experiment and focused on implementation strength to represent the quantity of academic detailing delivered as well as penetration into each station. Given the real-world nature of implementation, using the proportion of providers exposed to academic detailing enabled us to capture the implementation strength and its impact on naloxone prescribing. Combined with a fixed effects approach, we generated estimates that could be interpreted as casual if all assumptions are met.

In our secondary aim, we ran a series of subgroup analyses using different patient populations at risk for opioid overdose to test the sensitivity of our findings. Our conclusions were consistent when evaluating patients who were prescribed an opioid categorized as high risk, who received 50 MEDD or greater, and had a RIOSORD class ≥ 5. However, among patients who had an opioid use disorder diagnosis or were on methadone, the significance between the predictor of interest (proportion of providers exposed to academic detailing) and outcome (total count of naloxone prescriptions prescribed) was not significant. One possible explanation is that those patient groups that did not yield significant associations may have inherent characteristics that were not considered in these models. Secondly, pharmacists were excluded as providers, who make up 25% of our prescriber population. Not all pharmacists are considered providers at the VA and their duties were not easily determined from the current data. Moreover, pharmacists with prescribing authorization also wrote orders on behalf of other providers, which would have inflated their numbers. By removing pharmacists with prescribing authority, we reduced the

potential for misclassification and confounding with the number of naloxone prescriptions prescribed, which yielded conservative estimates that were unlikely to impact our conclusions.

Finally, the findings from our study were generated from the VA population, which has a greater overdose mortality rate compared to the general U.S. population.[3] Veterans have other comorbid conditions that differentiate them from the general population, and these findings may not be generalizable outside the VA population. Despite these limitations, the results of our study provide empirical support for academic detailing in increasing naloxone access at a large, integrated healthcare system. Other systems may benefit from these findings when deciding whether to implement academic detailing within their institutions or networks.

Conclusions

This was the first study to evaluate implementation strength on naloxone prescriptions prescribed at the VA. Stations with larger proportion of providers who received an OEND-specific academic detailing educational outreach visit had a greater monthly total count of naloxone prescriptions prescribed. Successful implementation of academic detailing is critical in getting naloxone prescriptions to veterans at risk for opioid overdose. Failure to implement academic detailing denies veterans at risk of opioid overdose from necessary treatment and minimizes the ability of the VA to fulfill President Lincoln's promise: "To care for him who shall have borne the battle, and for his widow, and his orphan." The insights gained from these findings will allow decision makers to generate academic detailing implementation plans that take into consideration the strength of the intervention in order to achieve meaningful outcomes.

Tables and Figures

Table 2.1. Characteristics of primary care providers at the Veterans Health Administration, September 2014 to December 2017.

Variable	Providers (N=5452)
Age (year), mean (SD)	54.4 (9.5)
Male, n (%)*	1944 (43.0%)
Primary Care Provider Type	
Physicians, n (%)	3940 (72.3%)
Physician assistants, n (%)	298 (5.5%)
Nurse practitioner, n (%)	1214 (22.3%)
Mental health providers, n (%)	59, (1.1%)

* 935 providers with missing data

Table 2.2. Baseline station-level characteristics at the Veterans Health Administration.

Variable	Mean	SD
PCP's Age (year) per station	54.91	2.47
Proportion PCP who are male per station	0.44	0.12
Proportion of PCP who are PA per station	0.06	0.07
Proportion of PCP who are NP per station	0.24	0.13
Proportion of PCP who are MH per station	0.01	0.04
Number of Outpatient visits per station	82,711	50,592
Number of Emergency department and Urgent care visits per station	1,657	1,103
Number of Inpatient admissions per station	508	395
Number of Prescription released per station	93,977	55,063

PCP, Primary Care Providers
PA, Physician Assistant
NP, Nurse Practitioner
MH, Mental Health Provider
SD, Standard Deviation

Table 2.3. Station baseline characteristics grouped by varying proportions of providers exposed to academic detailing.

Variable	Proportion of providers exposed to academic detailing*						
	0%	>0% to 25%	>25% to 50%	>50% to 75%	>75% to 100%		
N=	27	39	36	18	10	F stat†	p-value
PCP's Age (year) per station, mean (SD)	54.6 (2.5)	54.8 (2.3)	55.1 (2.6)	55.3 (2.5)	54.7 (2.9)	0.29	0.882
Proportion PCP who are male per station, mean (SD)	0.45 (0.12)	0.42 (0.11)	0.44 (0.10)	0.44 (0.15)	0.48 (0.12)	0.79	0.537
Proportion of PCP who are PA per station, mean (SD)	0.08 (0.08)	0.07 (0.08)	0.04 (0.06)	0.04 (0.06)	0.06 (0.10)	1.49	0.208
Proportion of PCP who are NP per station, mean (SD)	0.24 (0.12)	0.24 (0.12)	0.25 (0.13)	0.27 (0.16)	0.20 (0.10)	0.61	0.659
Proportion of PCP who are MH per station, mean (SD)	0.01 (0.02)	0.02 (0.06)	0.01 (0.03)	0.00 (0.02)	0.01 (0.03)	0.32	0.861
Number of Outpatient visits per station, mean (SD)	76,411 (60,272)	87,078 (48,477)	81,308 (47,138)	85,517 (54,499)	82,693 (42,343)	0.19	0.942
Number of Emergency department and Urgent care visits per station, mean (SD)	1,466 (1,159)	1,658 (1,047)	1,572 (1,001)	2,094 (1,401)	1,685 (890)	0.96	0.430
Number of Inpatient admissions per station, mean (SD)	502 (442)	536 (394)	496 (393)	490 (407)	494 (312)	0.07	0.991
Number of Prescription released per station, mean (SD)	86,865 (62,003)	95,108 (57,132)	91,730 (48,238)	104,402 (57,450)	98,089 (53,598)	0.30	0.877

* Proportions of providers exposed to academic detailing at the of the study period
†F-stat degrees of freedom is 129
PCP, Primary Care Providers
PA, Physician Assistant
NP, Nurse Practitioner
MH, Mental Health Provider
SD, Standard Deviation

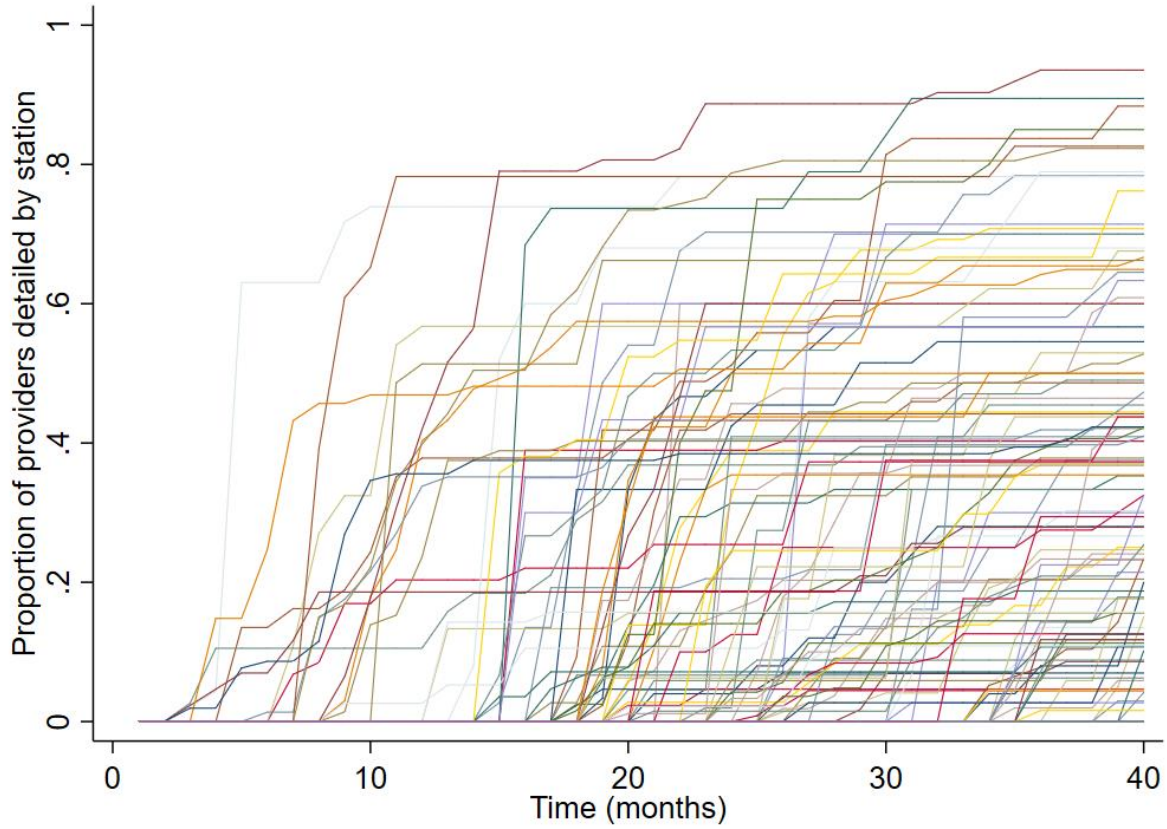
Table 2.4. Station-level results of the unconditional estimation fixed effects negative binomial regression models for different patient populations from September 2014 to December 2017.

Independent variables	(1) Negative binomial unconditional (Opioid population)	(2) Negative binomial unconditional (High risk population)	(3) Negative binomial unconditional (MEDD 50 population)	(4) Negative binomial unconditional (RIOSORD Class > 5 population)	(5) Negative binomial unconditional (OUD population)	(6) Negative binomial unconditional (Methadone population)
N	5200	5200	5200	5200	5197	5156
Time (month)	0.140*** (0.016)	0.128*** (0.015)	0.122*** (0.015)	0.174*** (0.029)	0.088*** (0.016)	0.085*** (0.022)
Proportion of providers exposed to academic detailing	**1.707** (0.552)**	**1.553** (0.514)**	**1.502** (0.533)**	**1.439** (0.657)**	0.853 (0.501)	1.368 (0.737)
Number of outpatient visits	-0.000 (0.000)	-0.000 (0.000)	-0.000 (0.000)	-0.000 (0.000)	-0.000 (0.000)	-0.000 (0.000)
Number of emergency department/urgent Care visits	-0.000 (0.000)	-0.000 (0.000)	0.000 (0.000)	-0.000 (0.000)	-0.000 (0.000)	0.000 (0.000)
Number of inpatient admissions	-0.000 (0.001)	-0.000 (0.001)	-0.000 (0.001)	0.000 (0.001)	0.000 (0.001)	-0.001 (0.001)
Number of prescriptions released	0.000** (0.000)	0.000** (0.000)	0.000*** (0.000)	0.000*** (0.000)	0.000* (0.000)	0.000 (0.000)
lnalpha	0.171* (0.082)	0.059 (0.088)	0.125 (0.089)	0.287*** (0.091)	-0.256* (0.130)	0.424 (0.130)
AIC	3.7742	3.4953	3.0967	2.6523	1.5190	1.1884
BIC	4.0605	3.7816	3.3830	2.9386	1.8054	1.4771
Average marginal effect	9.1293	5.2602	3.7545	4.2627	0.3950	0.4716
Delta method standard error	3.3418	1.8653	1.4251	2.1816	0.2348	0.2610

* p<0.05, ** p<0.01, *** p<0.001

Results are presented as the expected log count of naloxone with corresponding standard errors.

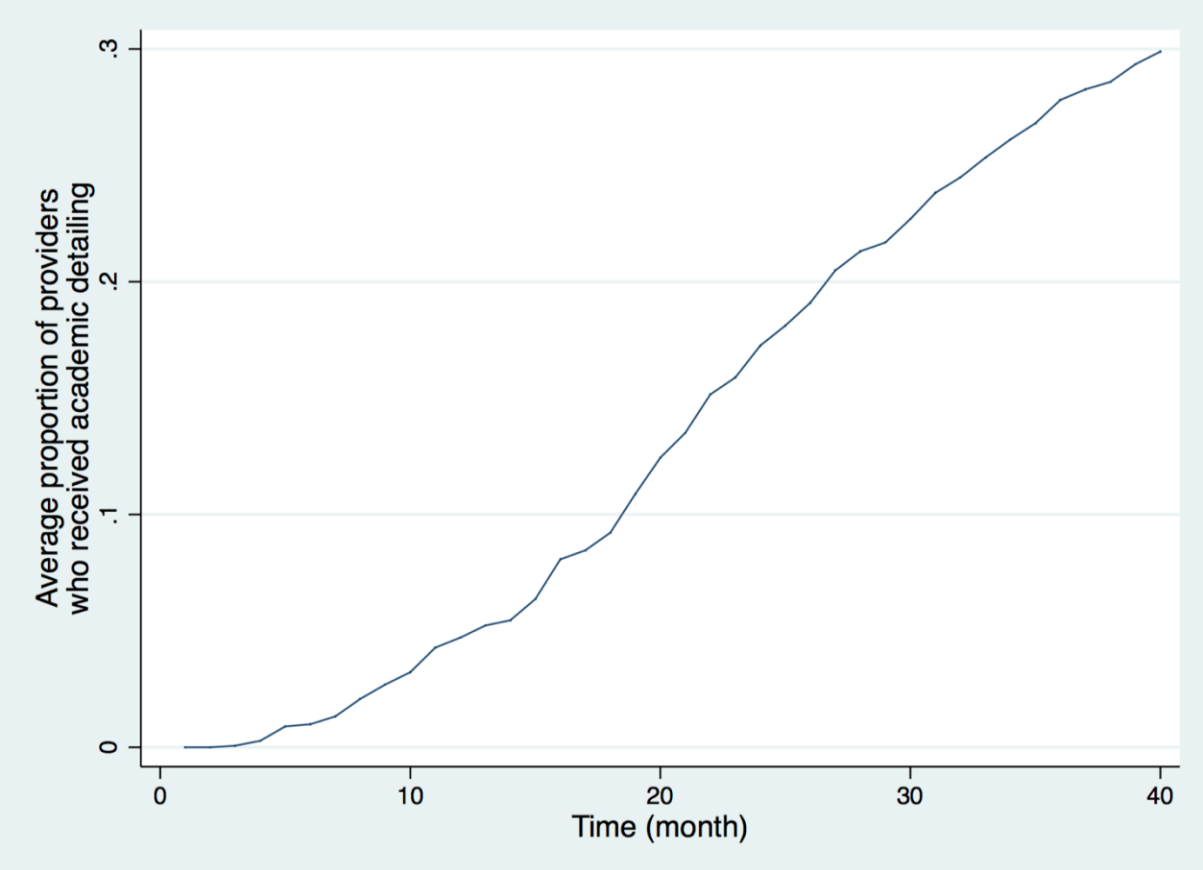
Figure 2.1. Proportion of providers exposed to OEND-specific academic detailing by station from September 2014 to December 2017.



Caption: Variation in implementation strength are visualized. Each line represented a VA station and the proportion of provider who received OEND-specific academic detailing educational outreach.

OEND, Opioid Overdose Education and Naloxone Distribution

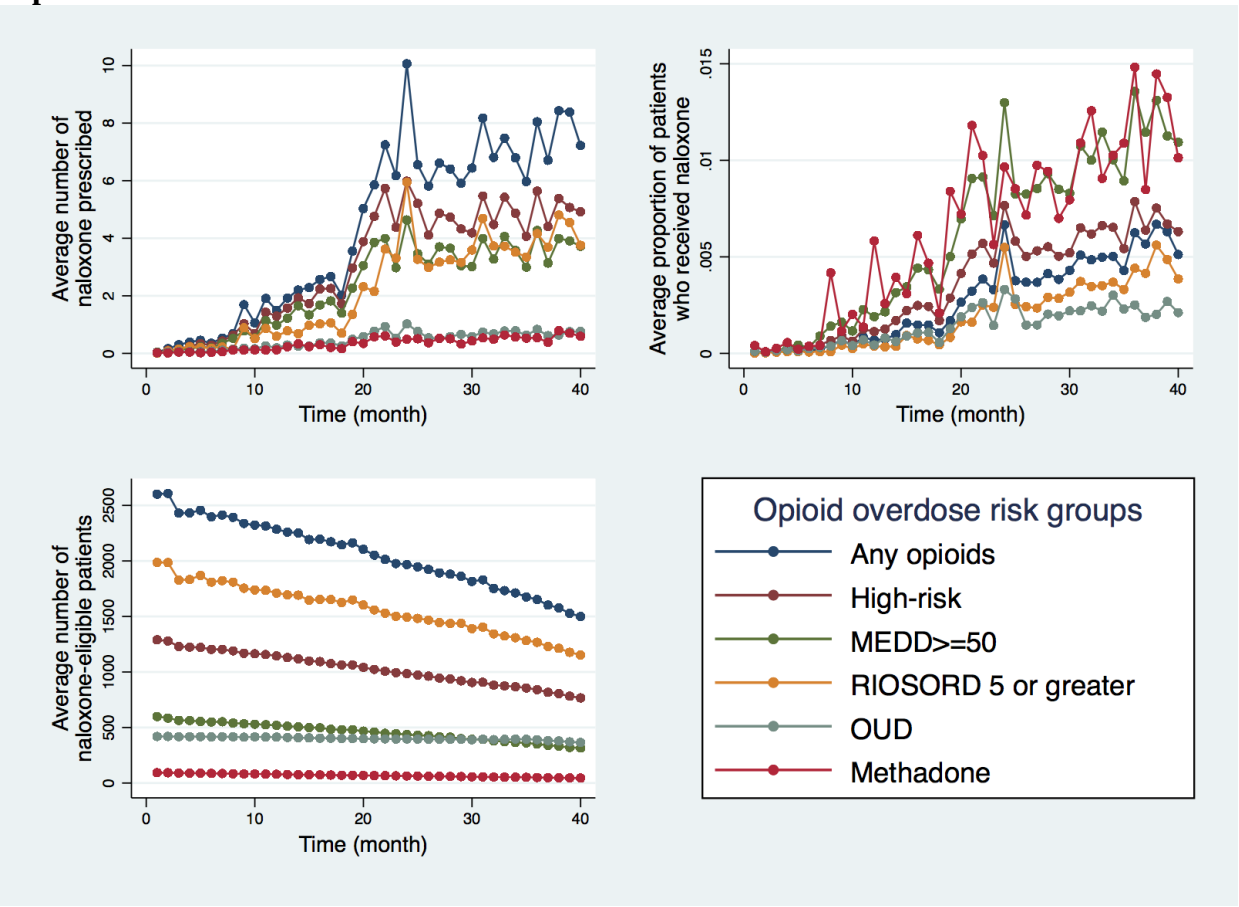
Figure 2.2. Average proportion of providers who received OEND-specific academic detailing from September 2014 to December 2017.



Caption: The overall average proportion of provider who received an OEND-specific academic detailing educational outreach visit was 0.14 across the study period with an overall standard deviation of 0.23 (range: 0.00 to 0.94).

OEND, Opioid Overdose Education and Naloxone Distribution

Figure 2.3. Monthly trends of average number of naloxone prescriptions prescribed, monthly average proportion of patients who received academic detailing, and the monthly average number of naloxone-eligible patients by different opioid overdose risk groups, September 2014 to December 2017.



MEDD, Morphine Equivalent Daily Dose
RIOSORD, Risk Index for Overdose or Serious Opioid-induced Respiratory Depression
OUD, Opioid Use Disorder

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Chapter 3: Providers' perceptions with academic detailing on opioid overdose education and naloxone prescribing behavior: A mixed methods design

Abstract

Background

Academic detailing is an educational outreach program that align providers' prescribing with evidence-based practice. The U.S. Department of Veterans Affairs (VA), in partnership with the Opioid Overdose Education and Naloxone Distribution Program, implemented the National Academic Detailing Service to deliver naloxone education to providers with patients at risk of opioid overdose. We conducted a study to explore elements of academic detailing that were important for augmenting naloxone prescribing.

Methods

A mixed methods approach using an online survey and semi-structured phone interview was used to explore providers' perceptions about academic detailing and naloxone prescribing at the VA. The online survey explored themes generated from existing theoretical frameworks using a 7-point Likert scale (1=Strongly disagree to 7=Strongly agree). Phone interviews were conducted to identify barriers and facilitators to naloxone prescribing.

Results

Overall, 137 (12.2%) providers completed the survey. Responders included primary care (51%), pain specialists (21%), and others types of providers (28%). The average domain score for responders was highest for Satisfaction (6.28) followed by Attitude (6.02), Knowledge (5.96), Social norms (5.64), and Perceived barriers (4.86). Knowledge, Social norms, and Satisfaction

domains were similar across the different provider types. However, pain specialists had a higher Attitude score (+0.56, P=0.011) and Perceived barriers score (+0.82, P=0.009) than primary care providers. A total of 11 responders participated in phone interviews. Participants identified limited time, poor data integration, social stigma, and lack of homeless support as barriers to prescribing naloxone. A patient list generated by academic detailers was identified as a facilitator to prescribing naloxone.

Conclusions

Providers were practicing at a level that was consistent with the VA goals to generate access to naloxone for opioid overdose; however, barriers continue to exist. Academic detailing will need to address issues of social stigma regarding naloxone, educate providers about support systems for homeless veterans, and develop tools for data integration.

Background

Opioid-related mortality has reached epidemic proportions in recent years. In 2015, 33,091 deaths were attributable to opioid-related drug overdoses with 46% of deaths due to prescription opioids (e.g., oxycodone, hydrocodone).[1] At greater risk are veterans who have twice the mortality rate for accidental drug overdose compared to the general United States (U.S.) population.[2] Naloxone, a Food and Drug Administration (FDA) approved drug used to reverse the effects of opioid-related overdose (e.g., respiratory depression), has been a critical part of an overall strategy adopted by the U.S. Department of Veterans Affairs (VA) to reduce opioid-related mortality through the development of the Opioid Overdose Education and Naloxone Distribution (OEND) Program. The VA implemented the OEND Program in 2014 to educate

patients and providers on opioid overdose prevention, recognition, and response, in particular with naloxone administration.[3] In order to provide OEND-specific educational outreach to providers, the OEND Program partnered with the VA Pharmacy Benefits Management Academic Detailing Service to conduct face-to-face sessions with providers.

Academic detailing is a multifaceted, educational outreach intervention that educates prescribers through interactions with academic detailers using evidence-based research, educational brochures, and clinical dashboards to align prescribing behavior with best practices via "key messages. "[4–6] In the VA, academic detailers (specially trained clinical pharmacists) identify prescribers using priority panels of high-risk patients, arrange one or more visits with prescribers, and share naloxone-prescribing data along with population management tools that highlight veterans at risk for opioid-related overdose.[7] Providers exposed to OEND-specific academic detailing are expected to adhere to naloxone prescribing guidelines, thereby increasing their rate of naloxone prescribing for veterans at high-risk of opioid-related overdose.

During the early days of the opioid crisis, the use of naloxone for opioid-related overdose was restricted to first responders. As state laws and public health program increased access to naloxone for patients at risk for opioid-related overdoses (including their family and friends), prevailing stigma, lack of knowledge surrounding naloxone, and illicit drug use contributed to further misunderstandings and barriers.[8–13] To better understand these barriers, several studies examined the knowledge, attitudes, and beliefs of providers and healthcare staff in regards to naloxone use to reverse opioid overdose in the outpatient setting. Binswanger and colleagues identified several barriers that contributed to naloxone prescribing resistance. These included

lack of knowledge, logistical/system barriers, and attitudinal and contextual concerns.[8] Peckham and colleagues similarly reported that providers identified lack of knowledge (e.g., opioid overdose education and naloxone prescribing) and fear of consequences (e.g., moral hazard) as barriers to the OEND Program implementation at the VA.[9] Academic detailing offers an opportunity to bridge the knowledge gaps and assuage these concerns by providing flexible, customizable OEND-specific educational outreach to providers with the goal of aligning them with naloxone-specific evidence-based practice.

To date, very little has been written about the relationship between providers' perceptions of academic detailing, the elements they find valuable, and whether these influence naloxone prescribing behaviors. Poor delivery by the academic detailers or distrust stemming from the targeted providers will likely result in poor adoptability of "key messages" resulting in low to no naloxone prescriptions for patients at risk for an opioid-related overdose.[14] There is also a paucity of data on the factors that providers identify as facilitators and barriers to adopting the OEND-specific key messages delivered by an academic detailer.

Therefore, we explored the themes that are associated with naloxone prescribing changes to explain the mechanisms responsible for academic detailing's effectiveness at augmenting providers' naloxone prescribing behavior. Findings from this study will allow us to develop a deeper understanding of the phenomena behind academic detailing in regards to opioid overdose education and naloxone prescribing at the VA.

Methods

Design

This was a mixed-methods study that used an online survey to capture providers' perception of academic detailing and naloxone use to reverse opioid-related overdose in the outpatient setting (Phase I) and semi-structured interviews with providers to capture facilitators and barriers to adoption of key messaged delivered by the academic detailer (Phase II).

The online survey was developed using existing theories of adoption of key messages and provider prescribing behavior changes, and was deployed to providers who recently received an OEND-specific academic detailing educational outreach visit. The survey evaluated themes that were associated with providers' self-stated changes in naloxone prescribing, improvement in naloxone-related knowledge, and changes in attitudes and beliefs regarding naloxone use in the outpatient setting to reverse opioid-related overdose events. Providers who completed the survey were asked to participate in the qualitative component (semi-structured interview) that involved a phone call to solicit additional themes related to facilitators and barriers to the adoption of key messages. The qualitative data were used to triangulate and complement the quantitative data, thus enriching our understanding of academic detailing.[15–18]

This national study was conducted at the VA between August 2017 to April 2018 and was reviewed and approved by the Institutional Review Boards at the Veterans Affairs San Diego Healthcare System (IRB #H170070) and the University of Washington (IRB# STUDY00004510).

Development of a conceptual framework

No single theory of adoption of "key messages" exists in the literature; however, there are several theoretical frameworks that have been used to conceptualize the adoption of key messages delivered by academic detailers. The social marketing framework,[19] the theory of planned behavior,[20] and the framework for effective implementation[21] have been reported to contribute to the overall theory of the adoption of "key messages" delivered by academic detailing.

In the context of academic detailing, the application of these frameworks provides a solid theoretical foundation to assess the behavioral actions of providers due to the educational outreach delivered by academic detailers. A conceptual framework was constructed using the elements from existing theoretical frameworks[19–21] to explain and understand the phenomena of academic detailing (**Figure 3.1**). Integrating these factors together, we proposed to identify areas where academic detailing is effective at delivering its "key messages" and to determine which factors influence providers' prescribing behavior, further expanding our understanding underlying these mechanisms.

Phase I: Online survey

Development of the online survey used in this study underwent several iterations (**Appendix A.3.1**). Initially, a draft online survey (Version 1.0) based on existing theories contained 42 items. Two experts in psychometric testing and survey development methods reviewed the draft online survey and provided feedback on item construction and cognition resulting in an updated draft (Version 2.0). This updated survey underwent two rounds of review by four experts in

academic detailing with a total combined experience of 15 years to reduce the number of items. The four experts met with the principal investigator (MB) of the study to discuss item selection for elimination. In the first round of review, item count was reduced from 42 to 33 (Version 3.0); and in the second round of review, this was further reduced from 33 to 26 (Final version). The final online survey was tested on six program managers from the Academic Detailing Service for face validity prior to deployment (Final survey available as **Appendix A.3.2**).

The online survey used a 7-point Likert scale (e.g., Strongly Agree, Agree, Somewhat Agree, Neutral, Somewhat Disagree, Disagree, and Strongly Disagree)[22] and contained 26 items that captured providers' perception of academic detailing and naloxone prescribing. Part of the survey contained 18 items across 5 domains: Attitude (4 items), Knowledge (3 items), Perceived barriers (5 items), Satisfaction (4 items), and Social norms (2 items). Other parts of the survey included eight additional items that captured the respondent's history of naloxone prescribing (1 item), the amount of time spent with the academic detailer (1 item), and whether the provider would recommend their colleagues see an academic detailer (2 items). Provider's self-stated changes were captured for improvement in knowledge (1 item), improvement in attitude (1 item), and self-reported naloxone prescribing change (2 items).

Online surveys were deployed using REDCap (Research Electronic Data Capture) electronic data capture tools hosted at the VA. REDCap is a secure, web-based application designed to support data capture for research studies.[23,24] An email invitation with instructions, consent form and authorization, and a link to the online survey instrument were sent to all eligible providers in the VA two to four weeks after the most recent OEND-specific academic detailing visit that took

place from August 2017 to April 2018. Follow-up reminders to providers were sent one-week after the initial email invitation for a total of three reminders. If the provider did not respond, they were coded as a non-responder.

Phase II: Semi-structured interview

Semi-structured phone interviews were conducted for the qualitative phase of the study (Phase II). An interview script was generated based on the perceived behavioral control domain (factors that facilitate or impeded naloxone prescribing) of the Theory of Planned Behavior (**Appendix A.3.3**). Each phone interview with a provider was estimated to range between 15 to 30 minutes and was conducted by the same research investigator (MB) to reduce variations between interviews. Prior to each interview, verbal consent was received from the provider. Phone interviews were captured using a voice recorder approved by the VA Information Security Office and stored on a secured VA terminal. Interviews were transcribed and de-identified by the VA Centralized Transcription Service Program (Salt Lake City, UT) and were stored using Atlas.ti version 7.0 (Scientific Software Development GmbH, Berlin, Germany).[25]

Sampling frame

Survey respondents in Phase I were selected using purposeful sampling based on the following criteria: (1) providers were selected if they received an OEND-specific academic detailing educational outreach visit and were active during the study period (August 2017 to April 2018) and (2) had an active VA email account.

In Phase II, providers were selected for an interview based on an item in the online survey instrument that asked providers if they would be interested in participating in the qualitative phase of the study (Phase II). Interviews were conducted until saturation was achieved.

Analysis

Phase I—Survey evaluation

Descriptive analyses were performed to describe the sample. Comparisons between primary care providers, specialists (substance use disorder and pain), and other providers were performed using one-way analysis of variance for continuous data and chi square test for discrete data. Scheffe multiple-comparison tests were performed for post hoc comparisons between Primary care, Specialists, and Others provider groups. We also performed demographic comparisons between responders and non-responders.

Multivariable logistic regression models were constructed to evaluate the association between improvement in naloxone-related knowledge, improvement in attitude about naloxone, and average domain scores with the self-stated changes to naloxone prescribing, controlling for provider baseline characteristics (**Appendix A.3.4**). The main predictors of interest included the binary variables for self-stated improvement in naloxone-related knowledge, self-stated improvement in attitude about naloxone, and continuous variables for each average domain score (Knowledge, Attitude, Social norms, Perceived barriers, and Satisfaction). A list of the binary dependent variable (self-stated changes in knowledge, attitude, and naloxone prescriptions prescribed) are summarized in **Table 3.1**. Forest plots on the odds ratio (OR) scale (with 95%

confidence intervals) were reported for models using binary and continuous predictors. **Table 3.2** summarizes the different logistic regression models performed.

Phase II—Semi-structured interviews

A modified grounded theory approach was used to explain how academic detailing affects a provider's naloxone prescribing behavior. Grounded theory begins by introducing existing knowledge of academic detailing and its impact on prescribing behavior to better understand how academic detailing can influence a provider's naloxone prescribing behavior, while allowing for emergent themes to be identified and incorporated into the overall theory.[26,27] Select narratives were presented to represent the emerging themes from the interviews.

An a priori codebook with predefined themes and constructs based on the conceptual framework was developed by the principal investigator (MB). Using this a priori codebook, two coders (MB and KS) independently reviewed early transcripts and convened to discuss their coding. During these early sessions, the coders were allowed to modify or introduce codes that matched to the themes and constructs from the conceptual framework. Following these discussions, a revised codebook was finalized and then applied to the remaining interview transcripts. If a new (de novo) code or theme was identified, the coders would re-review previous transcripts for any missed codes before reconvening to discuss. Any disagreements were resolved by consensus.

Results

Phase I—Online Survey Findings

A total of 137 (12.2% responders) out of 1,126 providers who had prescriptive authority at the VA completed the online survey (**Figure 3.2**). Non-responders were older [50 years (SD, 12) versus 47 years (SD, 12), P=0.0256] and mostly males (52% versus 36%; P=0.001) compared to responders. There were no significant differences in the average number outpatient visits [753 (SD, 567) versus 943 (SD, 1060); P=0.176] and patients seen (413 versus 132; P=0.165) one year prior to the survey deployment between non-responders and responders. Additionally, geographic distribution of non-responders and responders were similar across the VA (**Appendix A.3.5**).

Table 3 summarizes the demographics of providers who completed the survey. A majority of responders were primary care providers (51%) and female (69%). A large proportion of responders were physicians (41%), worked at the VA between 0 and 5 years (49%), and in practice between 11 and 15 years (44%). Approximately 57% of responders had written for naloxone prior to receiving the survey, and 51% received some form of naloxone training of which a large proportion (29%) received more than 12 months ago.

Figure 3.3 summarizes the average domain scores for the providers who completed the survey (higher score indicates greater agreement with the statements). In total, the average domain score for responders was highest for Satisfaction (mean=6.26, SD=1.03) followed by Attitude (6.02, 0.85), Knowledge (5.96, 0.75), Social norms (5.63, 1.07), and Perceived barriers (4.86, 1.22). No significant differences in average domain score was reported for the Knowledge, Social norms, and Satisfaction domains for the different provider types (**Appendix A.3.6**). However,

Specialists reported a higher average Attitude domain score (+0.56, P=0.011) and Perceived barriers domain score (+0.82, P=0.009) than Primary care providers.

We evaluated the impact of responders' *knowledge improvement* with their self-stated naloxone behavior changes (**Figure 3.4A**). Responders who stated that their knowledge improved after the academic detailing visit had greater odds of stating that they prescribed naloxone more frequently compared to responders who did not (OR=5.71; 95% CI: 1.92, 16.50). Responders who stated that their knowledge improved after the academic detailing visit had greater odds of stating that they used the information from the academic detailer to change their naloxone prescribing compared to responders who did not (6.29; 95% CI: 2.24, 17.62).

Similar findings were reported for responders who stated that their *attitude improved* after the academic detailing visit (**Figure 3.4B**). Responders who stated that their attitude improved had a 6.70 (95% CI: 2.55, 17.55) greater odds of increasing their naloxone prescribing frequency compared to responders who did not state that their attitude improved. For responders who stated that their attitude improved, their odds of using the information from the academic detailer to change their naloxone prescribing was 12.69 (95% CI: 4.58, 35.13) times greater than the odds of responders who did not state that their attitude improved.

We evaluated the average domain scores to the self-stated changed in naloxone prescribing and use of information from the academic detailer to change their naloxone prescribing adjusting for previous history of naloxone prescribing, work history, provider type, and previous naloxone training (**Figure 3.5**). In **Figure 3.5A**, the domain score for Social norms was positively

associated with the provider stating that they would prescribe naloxone more frequently (OR=3.37; 95% CI: 1.19, 9.55). No other domains were associated with prescribing naloxone more frequently. In **Figure 3.5B**, none of the domains were associated with the responders stating that would use the information from the academic detailer to change their naloxone prescribing.

Phase II—Interview results

According to Guest and colleagues, saturation ("the point at which no new information or themes are observed in the data") can be achieved within the first twelve interviews.[51,52] We were able to achieve saturation with 11 semi-structured interviews. The participants comprised of 6 physicians, 3 clinical psychiatric pharmacists, and 2 nurse practitioners; 81% were female. The average age was 49 years (range: 33 to 68).

We focused on the key findings of the barriers and facilitators for synthesizing information delivered by the academic detailer and for changing naloxone prescribing behavior.

<u>Perceived Barriers</u>

Participants identified stigma associated with naloxone as a barrier to prescribing. A pharmacist practitioner described how patients were reluctant to receive a naloxone prescription due to fears of being labelled an addict: "*[T]he main barrier I continue to hear, especially with our patients and even [medical] residents is the stigma that once they have a naloxone kit they will be labeled an addict*."

Participants also identified difficulty in writing naloxone prescriptions for homeless veterans without a support system. A pharmacist practitioner provided a description of this problem: "*So one of the negatives [is that] people will not give the kit…if the patient is homeless or [if] they don't have another individual in the appointment that can be educated at the same time of the education…I, personally, encourage them to share it with somebody (or even if they carry it). The instructions are in the kit so that doesn't stop me from prescribing it if the patient's okay with it. [S]ometimes I will see in the notes that providers won't give it because the patient doesn't have a support system at home*."

Participants also reported that they did not trust the accuracy of the information on the online clinical dashboard. As more data become available, finding time to validate and synthesize the information was burdensome. A pharmacist practitioner expressed frustration with disparate values when using the online clinical dashboards:
"*[T]here's so many different dashboards for OEND it's really confusing and when you want to use it for a specific task, it's really unclear which dashboard has the most accurate information because they will have varying numbers on the same thing sometimes*."

The same participant stated that they "*don't use them [clinical dashboards] often because we're not sure…how reliable they are*."

Participants expressed that they were unable to absorb and synthesize the wealth of information due to limited time. A pharmacist practitioner implied that clinical duties conflicted with her

available time to review the information delivered by the academic detailer and data on the online clinical dashboards:

"*[I]t's just a lot of data. It's been a lot better as we've continued to have more revisions and then there's, of course, like action plans that need to be done, but it's just a lot of information…to go through outside of your clinical duties*."

Online clinical dashboards do not appear to help participants in learning about their naloxone prescribing patterns. When asked about using the online clinical dashboard, a primary care physician admitted that they did "*not [use it] often. But randomly when something triggers me to think what's going on in my panel…or who on my panel has these particular clinical indicators*." Moreover, a pharmacist practitioner stated that:

"*Being a mental health pharmacist I don't use them much….I'm also on our Suboxone™ team and we're trying…to make sure with [name] and [name], there's so many different dashboards for OEND it's really confusing and when you want to use it for a specific task, it's really unclear which dashboard has the most accurate information because they will have varying numbers on the same thing sometimes*."

As more data are compiled and brought before providers, the time needed to sift through the information and develop trust in their accuracy and reliability is burdensome and creates obstacles to using these online clinical dashboards.

<u>Facilitators</u>

A patient list is generated by an academic detailer and presented to the provider in order to assess whether the patient should be on a naloxone prescription. Many participants expressed their appreciation when an academic detailer created a patient list to review specific cases. Participants pointed to the convenience of the patient list and how this streamlines their ability to prescribe naloxone to patients at risk for an opioid overdose. A nurse practitioner stated that:

"*I like that I can see what patients I have and what meds that they're on really easily because it's hard to sometimes even find a full list of my patients, let alone the ones that are on specific medications*."

Having a list also motivated participants to go through each patient and assess their naloxone prescription needs. For instance, a nurse practitioner described how a patient list generated by an academic detailer allowed her to identify patients and schedule them for a naloxone prescription:

"*[I] just sort of forged ahead and said, 'You know, I have a checkoff list. Well, I've got to get these 30 people done, let's just get them done.' So I just started scheduling them, come to clinic and…powering through it*."

Improvement

Participants were asked about improvements that would be needed to facilitate adoption of key messages delivered by the academic detailer and naloxone prescribing. A nurse practitioner stated that efficient integration of complex information was needed to synthesize all the data that providers are required to know before prescribing naloxone:

"*[O]ne day when we get our charts, either a new electronic medical record or something it'd be nice if it was integrated so that we could…go on and…see our patient and click on something*

and it would bring up the dashboard. Or, you know, something like that. So, without having to go to a separate program to pull that up."

A physician stated that having additional opioid-related information (urine drug screen results, opioid refills, and consent log) should be integrated into the naloxone electronic orders to help facilitate prescribing:

"*[T]he really useful thing for us on a day to day basis is that every time someone requests a refill we have…a note template that pulls to…a…consent on file for long term opioid use, it pulls the last [urinary drug screening] and it pulls the state [Prescription Monitoring Program] information. It does not pull if they have a Naloxone script I don't think*."

Additionally, the delivery of the key messages by the academic detailer was also identified for improvement. Although designed for one-on-one, face-to-face interactions, a physician stated that academic detailing should maintain the face-to-face interaction and shorten the educational materials:

"*I learn better by talking to someone than necessarily reading a bunch of pamphlets. I think if I was going to say anything I would probably say…they need to be shorter and just a few key points*."

Discussion

Providers' response to the online survey indicated that they were satisfied with their academic detailing experience, knowledgeable about naloxone prescribing and use, and supportive of naloxone access to patients at risk for opioid overdose, in addition to their family and friends.

Providers also indicated that their practice sites maintained a culture to improve naloxone access and meet with academic detailers about OEND. However, providers' responses to the online survey indicated that there were some barriers to prescribing naloxone.

Only Social norms was significantly associated with a self-stated change in naloxone prescribing after the academic detailing educational outreach visit. Providers who tended to agree with statements about their environment (in regards to naloxone prescribing and academic detailing) had higher odds of increasing naloxone prescribing. However, no other associations were identified with the other domains. This was unsurprising given the goal of the VA to improve providers' knowledge and attitude about pain management. More than half of the providers were already educated about naloxone prescribing prior to the academic detailing; and more than half already wrote for a naloxone prescription. These findings indicated that VA providers were quite familiar with, knowledgeable and aware of the opioid crisis and naloxone prescribing, and any incremental gain from academic detailing did not significantly affect their naloxone prescribing.

In our qualitative assessment, we focused on a few key barriers to adoption of OEND-specific key messages delivered by the academic detailer. From our phone interviews, we discovered that providers faced challenges discussing naloxone with their patients fearing that they may feel unjustly targeted as an addict. Social stigma against patients with substance use disorder can compromise patients' access to effective harm reduction treatment such as naloxone. For instance, Barry and colleagues performed a study on public attitudes about drug addiction and reported that respondents were against policies that would increase access to effective drug addiction treatment and were more willing to allow discriminatory practices against those with

drug addiction.[30] Moreover, responders viewed addiction as a moral failure further burdening society with this undesirable responsibility. Negative attitudes and perspectives about addiction generate unnecessary barriers to harm reduction treatment and dangerously limit the ability of the healthcare system to properly address the opioid crisis. Recently, the White House Opioid Summit on March 1st 2018 has brought awareness to the problem of opioid use disorder, which may have begun the process of destigmatization so that patients with substance use disorder can receive the proper care without fear of social reprisal.[31] Public policy needs to adopt a philosophy of harm reduction so that patients with opioid use disorder can seek treatment without the burden of society's moral judgement.

Providers also found it difficult to prescribe naloxone without a proper patient support system in place, in particular for homeless veterans who are more likely to have substance abuse and mental health problems than homeless nonveterans.[32] Although the VA has begun to provide primary care services to homeless veterans with support for substance use disorder, recovery, and treatment through the Homeless Patient Aligned Care Team (H-PACT) model, there remain gaps in care.[33,34] Regardless, increasing access to naloxone to reverse opioid overdose decreases the chance for overdose mortality and increases opportunity for substance use treatment. Ultimately, academic detailing will need to work with the H-PACT, raise awareness, and strategize how best to address these concerns through provider education.

In our interviews, providers felt overwhelmed by the large amount of data and tools (educational brochures and online clinical dashboards) that the academic detailer provided during the educational outreach visit. Limited time to synthesize the information and lack of integration

between the online clinical dashboards and the electronic medical records were barriers that prevented providers from maximizing the benefits from these tools. Similar findings were reported by a study on laboratory patient dashboard perceptions of medical residents at a single institution where medical residents indicated that a lack of time and integration were barriers to laboratory dashboard use.[35] Low engagement by providers at the VA are a reflection of the time constraints imposed on their clinical activities. Academic detailers can help reduce this burden by streamlining their delivery and generating patient lists from the complex data tools. In our interviews, providers expressed that the patient lists that academic detailer prepared for their educational outreach visit facilitated assessment and naloxone prescribing to patients at risk for opioid overdose. Having academic detailers review patients using an online clinical dashboard, synthesize the information, develop a list of priority patients at risk of opioid overdose, and sharing that with providers can facilitate access to naloxone.

Limitations

Despite sending three reminder emails starting one week after the online survey deployment to maximize the number of responders (Phase I), we only achieved a 12% response rate. Factors associated with low response include lack of monetary incentives[36,37] and survey length.[38,39] Frist, we were unable to offer financial incentives due to the regulations of the VA. But this should not matter since incentivizing providers to complete the survey can introduce response bias and create a feeling of coercion, which could yield untruthful responses. Moreover, the amount of incentive to providers experiences diminishing marginal returns after $50.[36,37] Second, providers have limited time and completing a lengthy survey competes with their other duties. Jepson and colleagues reported that an increase in 100 words was associated with an 11%

decrease in the odds of responding to a survey (95% CI: 3% and 19%).[39] Despite this limitation, the non-responders were similar in many characteristics to the responders suggesting no theoretical differences in responses.

Although face-to-face interviews are effective at establishing relationships early on and allow for clarification of questions and statements, they are costly, time intensive, and less effective at obtaining sensitive information.[40,41] A phone interview is advantageous because it does not require travel, is time-efficient, and has good reachability, thereby increasing the range of participants.[40–43] Arguments against phone interviews include a loss of rapport, loss of contextual data, and loss or distortion of non-verbal data.[43,44] However, these losses are balanced by the anonymity of a phone interview, which can reveal sensitive information that would, otherwise, not be forthcoming in a face-to-face interview.[40,45] In addition, phone interviews are focused and specific, which results in richer data.[43] Ultimately, our phone interviews were able to solicit themes that were not part of the conceptual framework and yielded important insight into barriers and facilitators to adoption of key messages delivered by the academic detailer.

We were unable to capture providers' perception before the academic detailing session because program implementation occurred prior to our evaluation. Consequently, we were unable to measure the change in domain scores pre-post academic detailing, which would have provided important information on academic detailing's impact on these domains. However, Winograd and colleagues reported that VA providers were concerned with iatrogenic patient behaviors and lacked knowledge about opioid overdose prior to the OEND Program at the VA.[13] Since the national implementation of the OEND Program, providers' perceptions about opioid overdose

and naloxone were expected to improve. In our study, we captured providers' current perceptions, which indicates that their knowledge, attitude, and perceived barriers were aligned with VA's expectations that they were well-informed, knowledgeable, and accountable for their patients' naloxone needs. Any incremental improvements in these domains did not yield significant effects on self-stated changes in naloxone prescribing.

Conclusions

VA providers were knowledgeable about academic detailing and naloxone prescribing for patients with opioid overdose risk, expressed attitudes and beliefs that aligned with evidence-based naloxone practice, and were satisfied with their interactions with academic detailers. Social norms significantly influenced their ability to write a naloxone prescription after meeting with an academic detailer. Additionally, providers identified limited time, poor data integration, social stigma, and lack of homeless patient support as barriers to writing a naloxone prescription for reversal of an opioid overdose. These findings will be used to improve the delivery of OEND-specific key messages to providers with the ultimate goal of generating access to harm reduction therapy, such as naloxone, for patients at risk of opioid overdose.

Tables and Figures

Table 3.1. Survey items on provider's self-stated changes.

Category	Item
Improvement in knowledge	My knowledge of naloxone increased after the academic detailing educational outreach visit
Improvement in attitude	After the academic detailing educational outreach visit, I felt more comfortable prescribing naloxone for opioid overdose in the outpatient setting
Changes to naloxone prescribing	Because of academic detailing, I prescribe naloxone more frequently
	I used the information from the academic detailer to change my naloxone prescribing practice

Table 3.2. Summary of logistic regression models.

Model	Type	Outcome	Predictors of interest	Covariates
1	Logistic	Increase naloxone prescribing (Yes/No)	Improvement in naloxone knowledge (Yes/No)	provider work history, previous naloxone prescribing, primary care, previous training in naloxone
2	Logistic	Increase naloxone prescribing (Yes/No)	Improvement in attitude about naloxone (Yes/No)	provider work history, previous naloxone prescribing, primary care, previous training in naloxone
3	Logistic	Used information from AD to change naloxone prescribing (Yes/No)	Improvement in naloxone knowledge (Yes/No)	provider work history, previous naloxone prescribing, primary care, previous training in naloxone
4	Logistic	Used information from AD to change naloxone prescribing (Yes/No)	Improvement in attitude about naloxone (Yes/No)	provider work history, previous naloxone prescribing, primary care, previous training in naloxone
5	Logistic	Increase naloxone prescribing (Yes/No)	Average domain scores*	provider work history, previous naloxone prescribing, primary care, previous training in naloxone
6	Logistic	Used information from AD to change naloxone prescribing (Yes/No)	Average domain scores*	provider work history, previous naloxone prescribing, primary care, previous training in naloxone

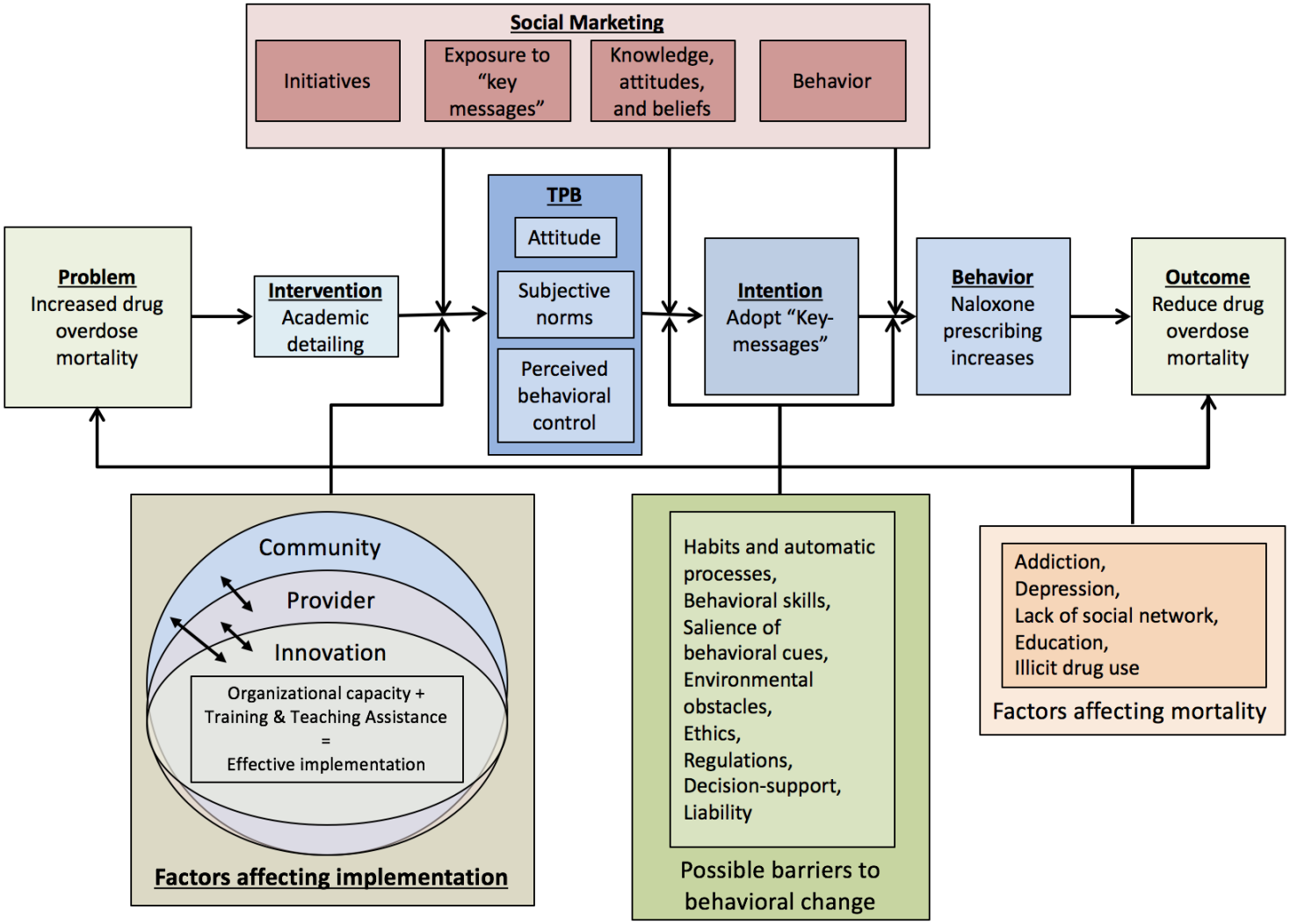
*Average domain scores included attitude, knowledge, perceived barriers, satisfaction, and social norms.

Table 3.3. Demographic characteristics of provider sample.

	Total (N=137)		Primary care (N=70)		Specialists (N=29)		Other (N=38)			
Variable	N	%	N	%	N	%	N	%	test statistic	p-value
Gender										
Male	42	31%	22	31%	7	24%	13	34%	0.825	0.662
Female	95	69%	48	69%	22	76%	25	66%		
Provider type										
Nurse practitioner	35	26%	17	24%	12	41%	8	21%		
Pharmacist practitioner	39	28%	19	27%	8	28%	10	26%	7.232	0.300
Physician	56	41%	31	44%	9	31%	16	42%		
Others	7	5%	3	4%	0	0%	4	11%		
How long have you been working at the VA?										
0-5 years	67	49%	41	59%	13	45%	13	34%		
6-10 years	26	19%	11	16%	5	17%	10	26%	5.587	0.134
11-15 years	14	10%	5	7%	5	17%	4	11%		
>15 years	30	22%	13	19%	6	21%	11	29%		
How long have you been in practice?										
0-5 years	33	19%	17	24%	10	34%	6	16%		
6-10 years	26	13%	15	21%	5	17%	6	16%	6.536	0.366
11-15 years	18	44%	6	9%	4	14%	8	21%		
>15 years	60	0%	32	46%	10	34%	18	47%		
Have you received any specific training (e.g., continuing education, certification, fellowship) on naloxone before the academic detailing visit?										
Yes	70	51%	35	50%	21	72%	14	37%	11.540	0.021
No	62	45%	34	49%	6	21%	22	58%		
Don't remember	5	4%	1	1%	2	7%	2	5%		
If you received training on naloxone before, approximately when did it occur?										
6 months ago	14	10%	7	10%	5	17%	2	5%	1.851	0.604
12 months ago	20	15%	13	19%	4	14%	3	8%		
> 12 months ago	40	29%	19	27%	11	38%	10	26%		
N/A	63	46%	31	44%	9	31%	23	61%		
Prior to academic detailing, have you written a prescription for naloxone?										
Yes	78	57%	42	60%	24	83%	12	32%	0.549	0.459
No	59	43%	28	40%	5	17%	26	68%		

Figures

Figure 3.1. Conceptual framework of the effect of academic detailing on naloxone prescribing.



TPB, Theory of planned behavior

Figure 3.2. Flow diagram used to determine the final responder sample.

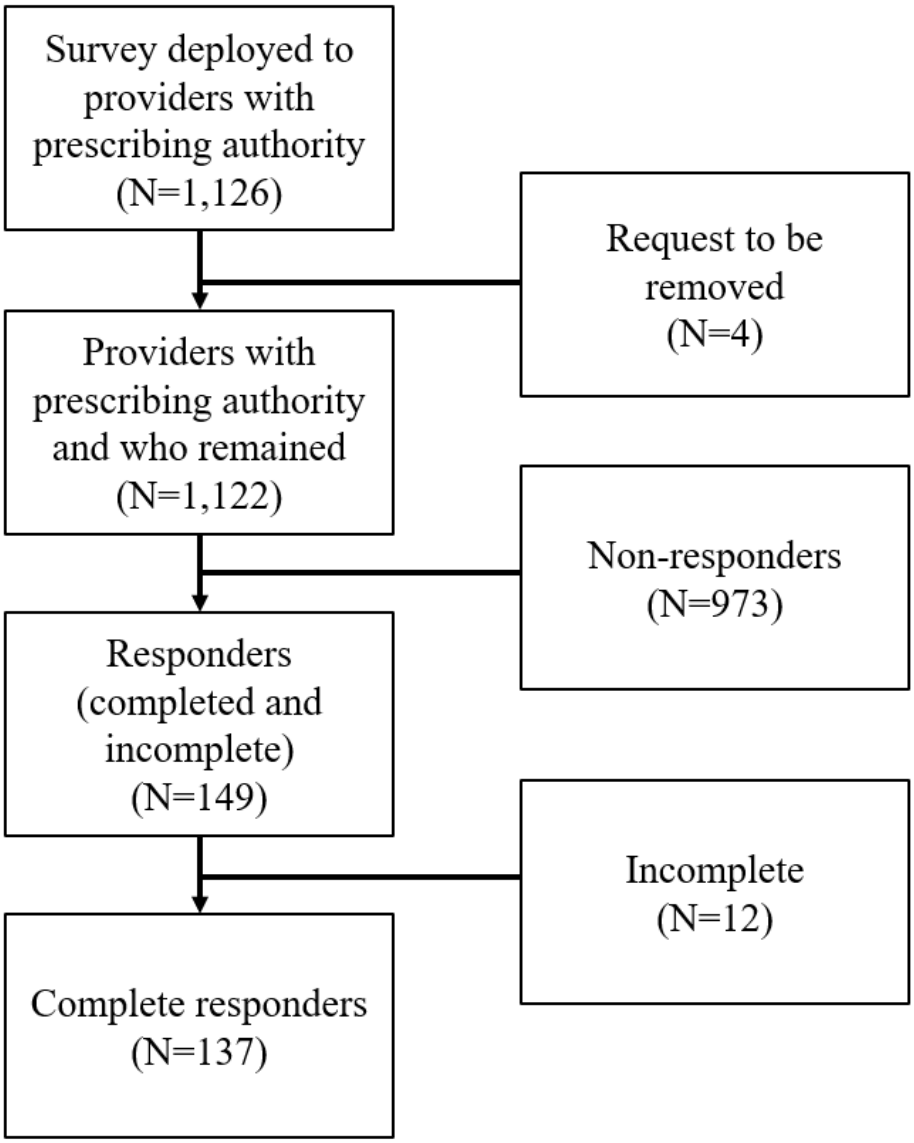
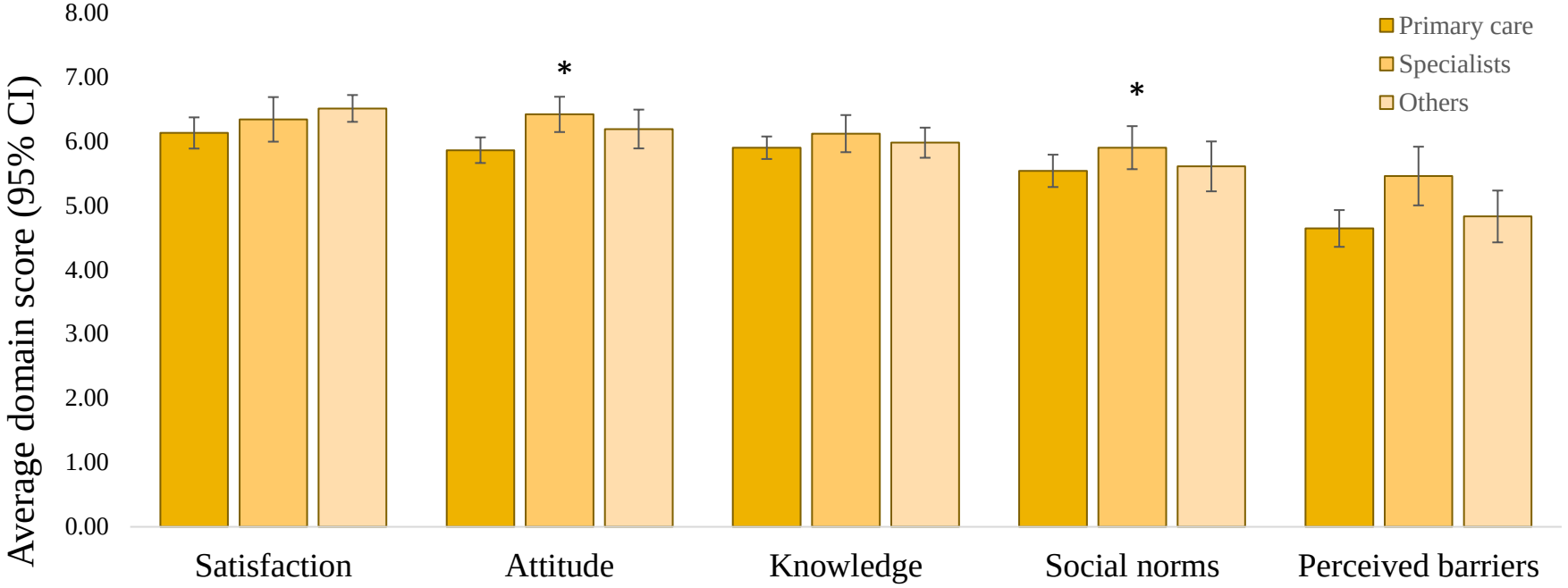
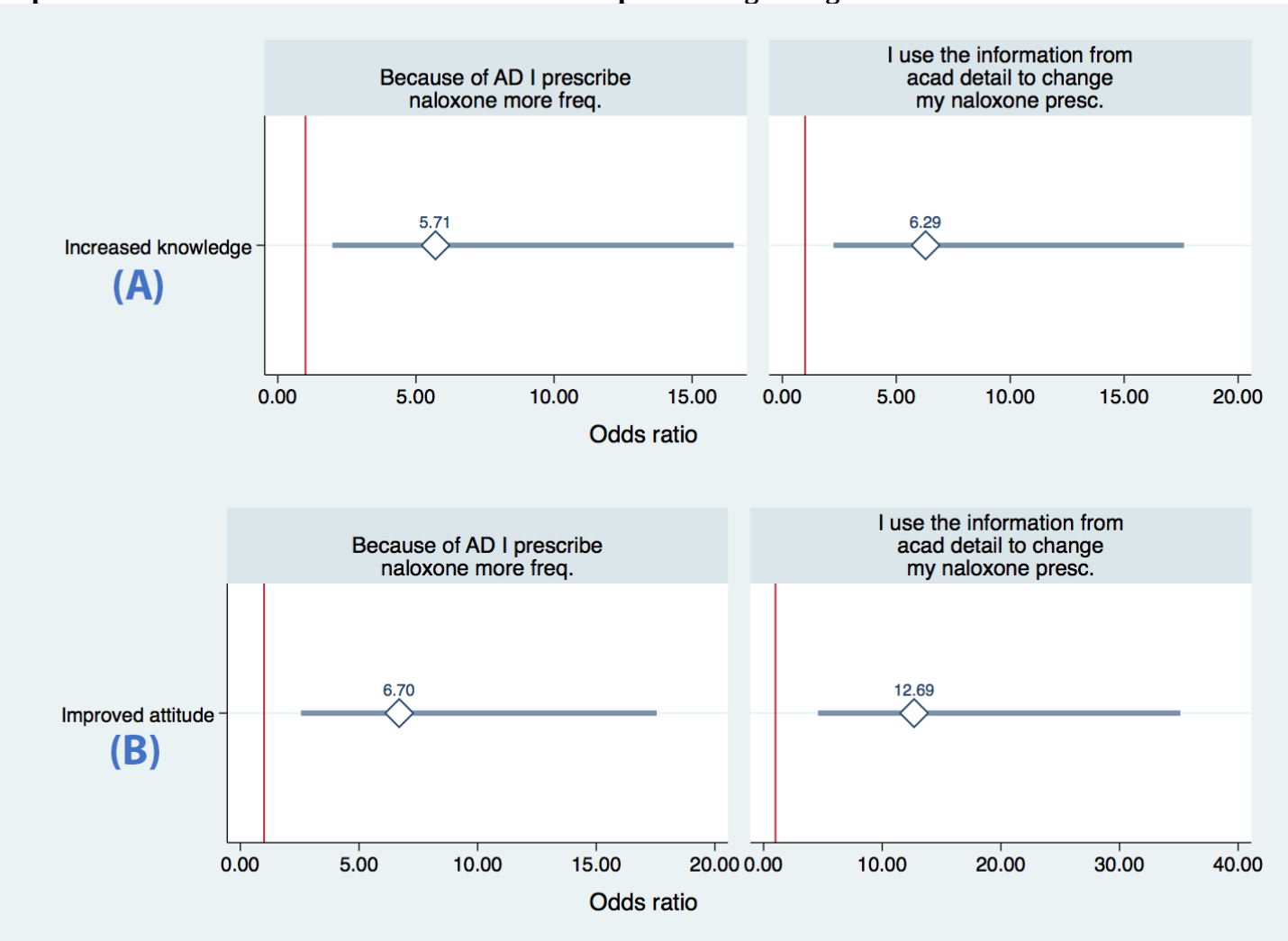


Figure 3.3. Average domain scores with 95% confidence intervals (CI) for responders who completed the online survey.



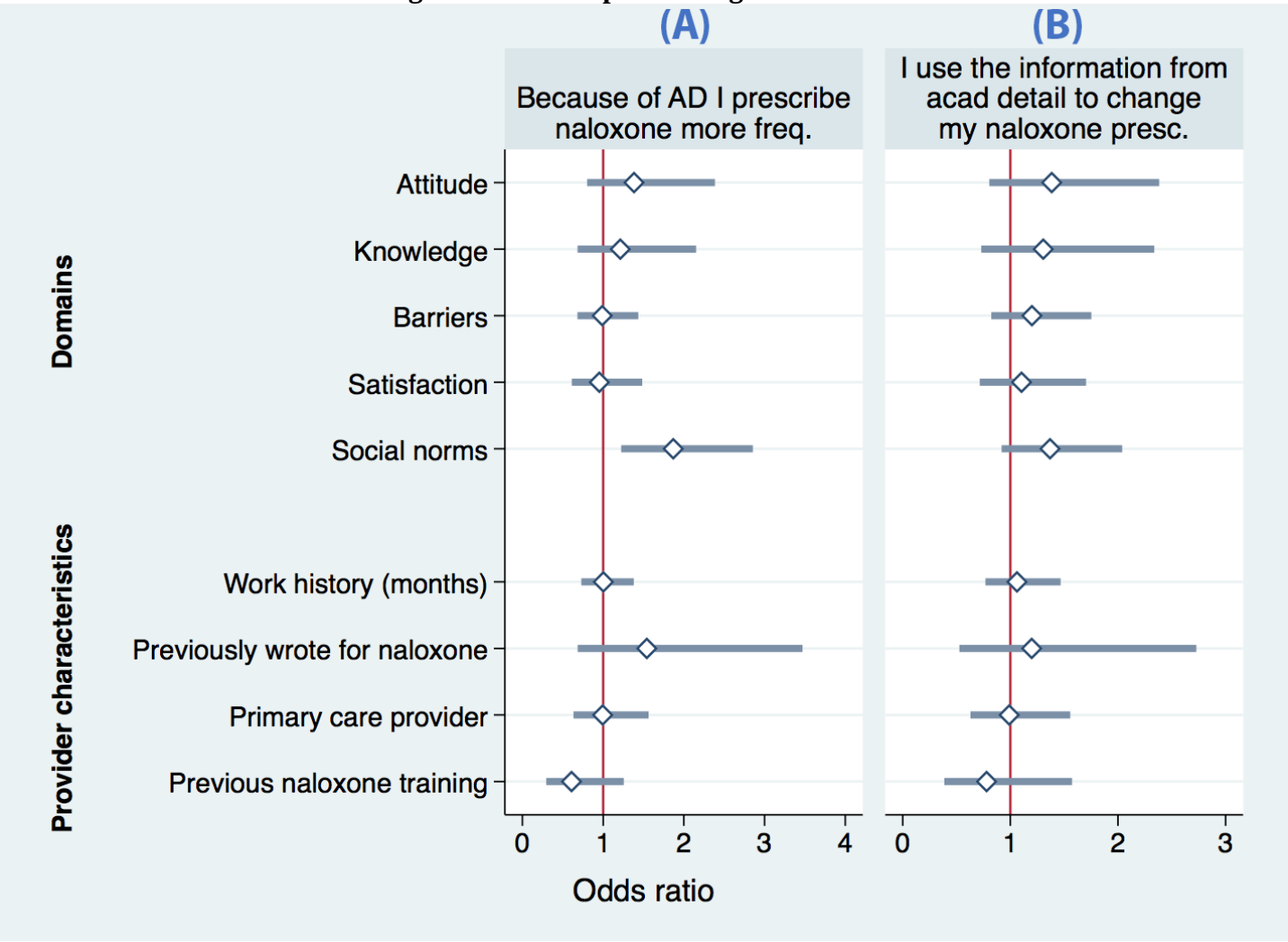
* p <0.05

Figure 3.4. Forest plots summarizing the odds ratio (OR) with 95% confidence intervals between increased knowledge and improvement in attitude with self-stated naloxone prescribing changes.



The vertical line represents the null (OR = 1). The models were adjusted for provider characteristics (work history, previous naloxone prescribing, primary care provider, previous naloxone training).

Figure 3.5. Forest plots summarizing the odds ratio (OR) with 95% confidence interval of domains and provider characteristics to self-stated changes in naloxone prescribing.



The vertical line represents the null (OR = 1).

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Chapter 4: Significance and Conclusions

Summary of findings

Implementation strength had an impact on academic detailing's effectiveness to increase naloxone prescriptions prescribed to reverse opioid overdose at the VA. Increasing the proportion of providers exposed to OEND-specific academic detailing educational outreach increased the number of naloxone prescriptions prescribed, which suggests that sites that do not maximize the number of providers receiving academic detailing will encounter a loss in their efficiency.

Providers who received academic detailing were knowledgeable, supportive, and worked at a practice site that maintained a culture to improve naloxone access and meeting with academic detailers. Providers who tended to agree with statements about their social norms (in regards to naloxone prescribing and academic detailing) had higher odds of increasing naloxone prescribing. These findings from the survey indicate that VA providers were knowledgeable and aware of the opioid crisis and naloxone prescribing, and any incremental gain from academic detailing did not significantly affect their naloxone prescribing.

Significance to practice

Addressing the opioid crisis at the VA has become a national priority and requires a multifaceted strategy to achieve.[32] Although the VA has implemented the Opioid Safety Initiate, its goal solely focuses on reducing opioid utilization.[33] A harm reduction strategy using naloxone is another critical part of the overall strategy to address the opioid crisis in a veteran population that is at twice the risk of overdose mortality.[3] A previous study reported that academic detailing in

partnership with the OEND Program was able to educate providers and improve access to naloxone for reversal of opioid-related overdose in veterans.[53] This indicated that direct educational outreach by an academic detailer can motivate a provider to change their prescribing behavior. However, implementation of academic detailer was an important process to achieving that has not been evaluated.

This dissertation was able to empirically support the idea that increased implementation strength (proportion of providers exposed to academic detailing) has a positive association with the number of naloxone prescriptions prescribed at each VA station. For decision makers, this finding indicates that VA stations have not maximized access to naloxone for veterans at risk for opioid overdose. Despite the Interim Under Secretary of Health mandating that all VA stations implement academic detailing, there are stations that have not sufficiently met this mandate thereby necessitating further plans to address this issue. Currently, the VA National Academic Detailing Service is developing plans to use telehealth to reach providers in rural areas to increase penetration. However, this plan will require careful implementation and evaluation to assess if naloxone prescribing will be impacted.

From our interviews, providers expressed appreciation of patient lists as a major facilitator for prescribing naloxone. Providers are required to synthesize an overwhelming amount of data in a limited time that any intervention that increases their efficiency is welcome. Academic detailers improved the providers' workflow by identifying patients at risk for opioid overdose, effectively saving time. However, lack of data integration, stigma, and patient support continue to be barriers to naloxone prescribing. Therefore, academic detailers will need to develop

collaborations with other disciplines and programs to address these issues and generate access to naloxone for veterans at risk for opioid overdose.

Conclusions

Implementation is an important element that should be considered as part of the program evaluation. In this dissertation, I provided evidence that increased implementation was associated with increased naloxone prescribing at the VA. Additionally, constructing a conceptual framework to explain the phenomena of academic detailing allowed me to explore themes associated with providers' naloxone prescribing behavior. My findings have deepened my understanding of how and why academic detailer works, which will allow me to improve the delivery of key message for future campaigns. Overall, the intersection of these two aims provides a narrative that supports the theory that targeted, educational outreach in OEND can align providers with evidence-based practice. More importantly, the emerging themes from the interviews provide a reminder that programs need to be evaluated and improved in order to be sustainable.

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Appendix

Appendix A.2.1 List of diagnostic codes used to identify patients.

ICD Version	ICD Code	ICD Description
9	304	Opioid type dependence unspecified
9	304	Heroin dependence unspecified
9	304.001	Methadone dependence unspecified
9	304.002	Morphine dependence unspecified
9	304.003	Opium dependence unspecified
9	304.009	Other opioid dependence unspecified
9	304.01	Opioid type dependence continuous
9	304.01	Heroin dependence continuous
9	304.011	Methadone dependence continuous
9	304.012	Morphine dependence continuous
9	304.013	Opium dependence continuous
9	304.019	Other opioid dependence continuous
9	304.02	Opioid type dependence episodic
9	304.02	Heroin dependence episodic
9	304.021	Methadone dependence episodic
9	304.022	Morphine dependence episodic
9	304.023	Opium dependence episodic
9	304.029	Other opioid dependence episodic
9	304.03	Opioid type dependence in remission
9	304.03	Heroin dependence in remission
9	304.031	Methadone dependence in remission
9	304.032	Morphine dependence in remission
9	304.033	Opium dependence in remission
9	304.039	Other opioid dependence in remission
9	304.09	Other opioid type depen, nec
9	304.7	Combinations of opioid type drug with any other drug dependence, unspecified use
9	304.71	Combinations of opioid type drug with any other drug dependence, continuous use
9	304.72	Combinations of opioid type drug with any other drug dependence, episodic use
9	304.73	Combinations of opioid type drug with any other drug dependence, in remission
9	305.5	Opioid abuse unspecified
9	305.5	Heroin abuse unspecified
9	305.501	Methadone abuse unspecified
9	305.502	Morphine abuse unspecified
9	305.503	Opium abuse unspecified
9	305.509	Other opioid abuse nec unspecified
9	305.51	Opioid abuse continuous
9	305.51	Heroin abuse continuous
9	305.511	Methadone abuse continuous
9	305.512	Morphine abuse continuous
9	305.513	Opium abuse continuous
9	305.519	Other opioid abuse nec continuous
9	305.52	Opioid abuse episodic
9	305.52	Heroin abuse episodic
9	305.521	Methadone abuse episodic
9	305.522	Morphine abuse episodic

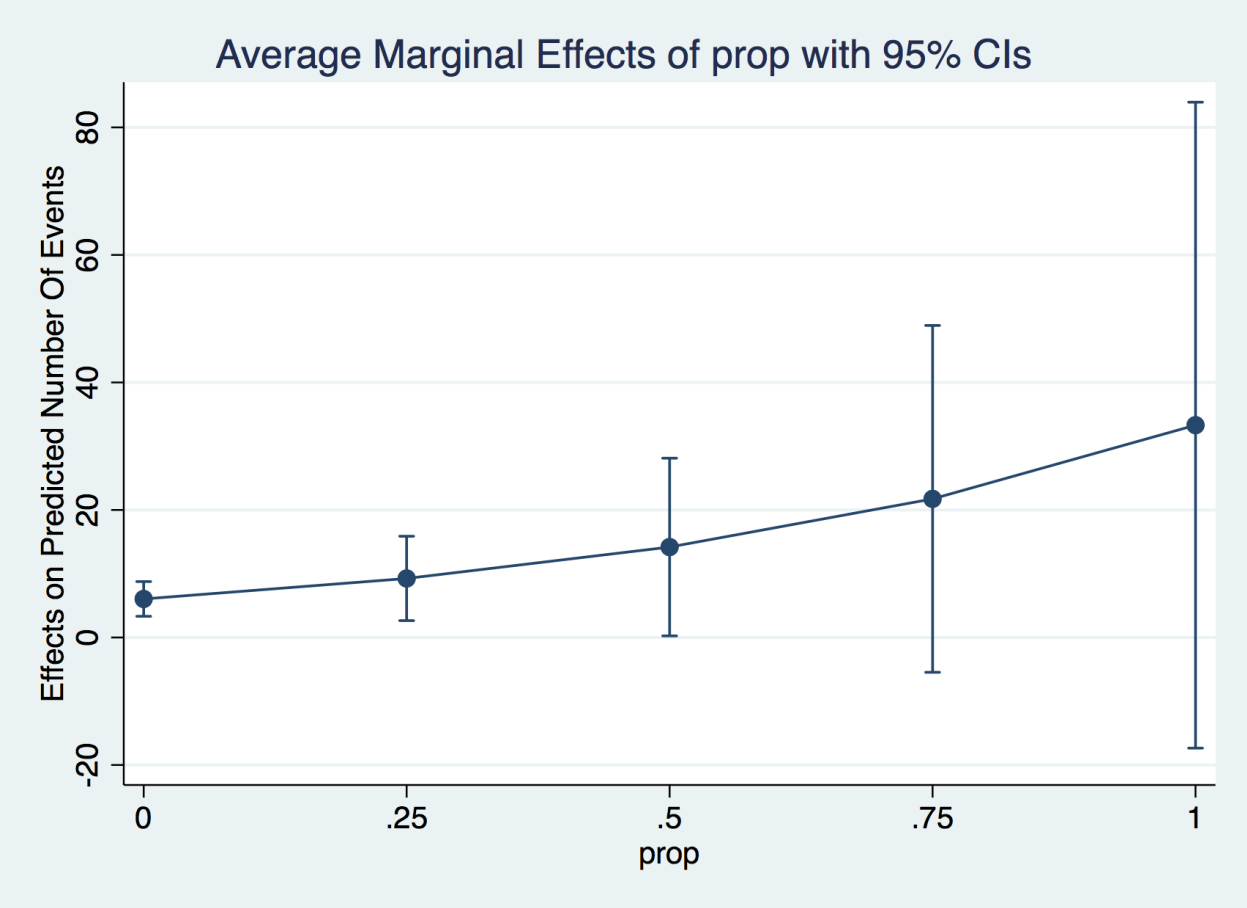
9	305.523	Opium abuse episodic
9	305.529	Other opioid abuse nec episodic
9	305.53	Opioid abuse in remission
9	305.53	Heroin abuse in remission
9	305.531	Methadone abuse in remission
9	305.532	Morphine abuse in remission
9	305.533	Opium abuse in remission
9	305.539	Other opioid abuse nec in remission
9	305.59	Other opioid abuse, nec
9	965	Poisoning by opium (alkaloids), unspecified
9	965.01	Poisoning by heroin
9	965.02	Poisoning by methadone
9	965.09	Poisoning by other opiates and related narcotics
9	E850.0	Accidental poisoning by heroin
9	E850.1	Accidental poisoning by methadone
9	E850.2	Accidental poisoning by other opiates and related narcotics
9	E935.0	Heroin causing adverse effects in therapeutic use
9	E935.1	Methadone causing adverse effects in therapeutic use
9	E935.2	Other opiates and related narcotics causing adverse effects in therapeutic use
9	E950.0	Suicide and self-inflicted poisoning by analgesics, antipyretics, and antirheumatics
9	E950.01	Suicide attempted by analgesics/antipyretics/antirheumatics
9	E950.02	Suicide actual by analgesics/antipyretics/antirheumatics
9	E980.0	Poisoning by analgesics, antipyretics, and antirheumatics, undetermined whether accidentally or purposely inflicted
10	F11.10	Opioid abuse, uncomplicated
10	F11.11	Opioid abuse, in remission
10	F11.120	Opioid abuse with intoxication, uncomplicated
10	F11.121	Opioid abuse with intoxication delirium
10	F11.122	Opioid abuse with intoxication with perceptual disturbance
10	F11.129	Opioid abuse with intoxication, unspecified
10	F11.14	Opioid abuse with opioid-induced mood disorder
10	F11.150	Opioid abuse with opioid-induced psychotic disorder with delusions
10	F11.151	Opioid abuse with opioid-induced psychotic disorder with hallucinations
10	F11.159	Opioid abuse with opioid-induced psychotic disorder, unspecified
10	F11.181	Opioid abuse with opioid-induced sexual dysfunction
10	F11.182	Opioid abuse with opioid-induced sleep disorder
10	F11.188	Opioid abuse with other opioid-induced disorder
10	F11.19	Opioid abuse with unspecified opioid-induced disorder
10	F11.20	Opioid dependence, uncomplicated
10	F11.21	Opioid dependence, in remission
10	F11.220	Opioid dependence with intoxication, uncomplicated
10	F11.221	Opioid dependence with intoxication delirium
10	F11.222	Opioid dependence with intoxication with perceptual disturbance
10	F11.229	Opioid dependence with intoxication, unspecified
10	F11.23	Opioid dependence with withdrawal
10	F11.24	Opioid dependence with opioid-induced mood disorder
10	F11.250	Opioid dependence with opioid-induced psychotic disorder with delusions
10	F11.251	Opioid dependence with opioid-induced psychotic disorder with hallucinations
10	F11.259	Opioid dependence with opioid-induced psychotic disorder, unspecified
10	F11.281	Opioid dependence with opioid-induced sexual dysfunction
10	F11.282	Opioid dependence with opioid-induced sleep disorder

10	F11.288	Opioid dependence with other opioid-induced disorder
10	F11.29	Opioid dependence with unspecified opioid-induced disorder
10	F11.90	Opioid use, unspecified, uncomplicated
10	F11.920	Opioid use, unspecified with intoxication, uncomplicated
10	F11.921	Opioid use, unspecified with intoxication delirium
10	F11.922	Opioid use, unspecified with intoxication with perceptual disturbance
10	F11.929	Opioid use, unspecified with intoxication, unspecified
10	F11.93	Opioid use, unspecified with withdrawal
10	F11.94	Opioid use, unspecified with opioid-induced mood disorder
10	F11.950	Opioid use, unspecified with opioid-induced psychotic disorder with delusions
10	F11.951	Opioid use, unspecified with opioid-induced psychotic disorder with hallucinations
10	F11.959	Opioid use, unspecified with opioid-induced psychotic disorder, unspecified
10	F11.981	Opioid use, unspecified with opioid-induced sexual dysfunction
10	F11.982	Opioid use, unspecified with opioid-induced sleep disorder
10	F11.988	Opioid use, unspecified with other opioid-induced disorder
10	F11.99	Opioid use, unspecified with unspecified opioid-induced disorder
10	R78.1	Finding of opiate drug in blood
10	T40.0X1A	Poisoning by opium, accidental (unintentional), initial encounter
10	T40.0X1D	Poisoning by opium, accidental (unintentional), subsequent encounter
10	T40.0X1S	Poisoning by opium, accidental (unintentional), sequela
10	T40.0X2A	Poisoning by opium, intentional self-harm, initial encounter
10	T40.0X2D	Poisoning by opium, intentional self-harm, subsequent encounter
10	T40.0X2S	Poisoning by opium, intentional self-harm, sequela
10	T40.0X3A	Poisoning by opium, assault, initial encounter
10	T40.0X3D	Poisoning by opium, assault, subsequent encounter
10	T40.0X3S	Poisoning by opium, assault, sequela
10	T40.0X4A	Poisoning by opium, undetermined, initial encounter
10	T40.0X4D	Poisoning by opium, undetermined, subsequent encounter
10	T40.0X4S	Poisoning by opium, undetermined, sequela
10	T40.0X5A	Adverse effect of opium, initial encounter
10	T40.0X5D	Adverse effect of opium, subsequent encounter
10	T40.0X5S	Adverse effect of opium, sequela
10	T40.1X1A	Poisoning by heroin, accidental (unintentional), initial encounter
10	T40.1X1D	Poisoning by heroin, accidental (unintentional), subsequent encounter
10	T40.1X1S	Poisoning by heroin, accidental (unintentional), sequela
10	T40.1X2A	Poisoning by heroin, intentional self-harm, initial encounter
10	T40.1X2D	Poisoning by heroin, intentional self-harm, subsequent encounter
10	T40.1X2S	Poisoning by heroin, intentional self-harm, sequela
10	T40.1X3A	Poisoning by heroin, assault, initial encounter
10	T40.1X3D	Poisoning by heroin, assault, subsequent encounter
10	T40.1X3S	Poisoning by heroin, assault, sequela
10	T40.1X4A	Poisoning by heroin, undetermined, initial encounter
10	T40.1X4D	Poisoning by heroin, undetermined, subsequent encounter
10	T40.1X4S	Poisoning by heroin, undetermined, sequela
10	T40.2X1A	Poisoning by other opioids, accidental (unintentional), initial encounter
10	T40.2X1D	Poisoning by other opioids, accidental (unintentional), subsequent encounter
10	T40.2X1S	Poisoning by other opioids, accidental (unintentional), sequela
10	T40.2X2A	Poisoning by other opioids, intentional self-harm, initial encounter
10	T40.2X2D	Poisoning by other opioids, intentional self-harm, subsequent encounter
10	T40.2X2S	Poisoning by other opioids, intentional self-harm, sequela

10	T40.2X3A	Poisoning by other opioids, assault, initial encounter
10	T40.2X3D	Poisoning by other opioids, assault, subsequent encounter
10	T40.2X3S	Poisoning by other opioids, assault, sequela
10	T40.2X4A	Poisoning by other opioids, undetermined, initial encounter
10	T40.2X4D	Poisoning by other opioids, undetermined, subsequent encounter
10	T40.2X4S	Poisoning by other opioids, undetermined, sequela
10	T40.2X5A	Adverse effect of other opioids, initial encounter
10	T40.2X5D	Adverse effect of other opioids, subsequent encounter
10	T40.2X5S	Adverse effect of other opioids, sequela
10	T40.2X6A	Underdosing of other opioids, initial encounter
10	T40.2X6D	Underdosing of other opioids, subsequent encounter
10	T40.2X6S	Underdosing of other opioids, sequela
10	T40.3X1A	Poisoning by methadone, accidental (unintentional), initial encounter
10	T40.3X1D	Poisoning by methadone, accidental (unintentional), subsequent encounter
10	T40.3X1S	Poisoning by methadone, accidental (unintentional), sequela
10	T40.3X2A	Poisoning by methadone, intentional self-harm, initial encounter
10	T40.3X2D	Poisoning by methadone, intentional self-harm, subsequent encounter
10	T40.3X2S	Poisoning by methadone, intentional self-harm, sequela
10	T40.3X3A	Poisoning by methadone, assault, initial encounter
10	T40.3X3D	Poisoning by methadone, assault, subsequent encounter
10	T40.3X3S	Poisoning by methadone, assault, sequela
10	T40.3X4A	Poisoning by methadone, undetermined, initial encounter
10	T40.3X4D	Poisoning by methadone, undetermined, subsequent encounter
10	T40.3X4S	Poisoning by methadone, undetermined, sequela
10	T40.3X5A	Adverse effect of methadone, initial encounter
10	T40.3X5D	Adverse effect of methadone, subsequent encounter
10	T40.3X5S	Adverse effect of methadone, sequela
10	T40.3X6A	Underdosing of methadone, initial encounter
10	T40.3X6D	Underdosing of methadone, subsequent encounter
10	T40.3X6S	Underdosing of methadone, sequela
10	T40.4X1A	Poisoning by other synthetic narcotics, accidental (unintentional), initial encounter
10	T40.4X1D	Poisoning by other synthetic narcotics, accidental (unintentional), subsequent encounter
10	T40.4X1S	Poisoning by other synthetic narcotics, accidental (unintentional), sequela
10	T40.4X2A	Poisoning by other synthetic narcotics, intentional self-harm, initial encounter
10	T40.4X2D	Poisoning by other synthetic narcotics, intentional self-harm, subsequent encounter
10	T40.4X2S	Poisoning by other synthetic narcotics, intentional self-harm, sequela
10	T40.4X3A	Poisoning by other synthetic narcotics, assault, initial encounter
10	T40.4X3D	Poisoning by other synthetic narcotics, assault, subsequent encounter
10	T40.4X3S	Poisoning by other synthetic narcotics, assault, sequela
10	T40.4X4A	Poisoning by other synthetic narcotics, undetermined, initial encounter
10	T40.4X4D	Poisoning by other synthetic narcotics, undetermined, subsequent encounter
10	T40.4X4S	Poisoning by other synthetic narcotics, undetermined, sequela
10	T40.4X5A	Adverse effect of other synthetic narcotics, initial encounter
10	T40.4X5D	Adverse effect of other synthetic narcotics, subsequent encounter
10	T40.4X5S	Adverse effect of other synthetic narcotics, sequela
10	T40.601A	Poisoning by unspecified narcotics, accidental (unintentional), initial encounter
10	T40.601D	Poisoning by unspecified narcotics, accidental (unintentional), subsequent encounter
10	T40.601S	Poisoning by unspecified narcotics, accidental (unintentional), sequela
10	T40.602A	Poisoning by unspecified narcotics, intentional self-harm, initial encounter
10	T40.602D	Poisoning by unspecified narcotics, intentional self-harm, subsequent encounter

10	T40.602S	Poisoning by unspecified narcotics, intentional self-harm, sequela
10	T40.603A	Poisoning by unspecified narcotics, assault, initial encounter
10	T40.603D	Poisoning by unspecified narcotics, assault, subsequent encounter
10	T40.603S	Poisoning by unspecified narcotics, assault, sequela
10	T40.604A	Poisoning by unspecified narcotics, undetermined, initial encounter
10	T40.604D	Poisoning by unspecified narcotics, undetermined, subsequent encounter
10	T40.604S	Poisoning by unspecified narcotics, undetermined, sequela
10	T40.605A	Adverse effect of unspecified narcotics, initial encounter
10	T40.605D	Adverse effect of unspecified narcotics, subsequent encounter
10	T40.605S	Adverse effect of unspecified narcotics, sequela
10	T40.691A	Poisoning by other narcotics, accidental (unintentional), initial encounter
10	T40.691D	Poisoning by other narcotics, accidental (unintentional), subsequent encounter
10	T40.691S	Poisoning by other narcotics, accidental (unintentional), sequela
10	T40.692A	Poisoning by other narcotics, intentional self-harm, initial encounter
10	T40.692D	Poisoning by other narcotics, intentional self-harm, subsequent encounter
10	T40.692S	Poisoning by other narcotics, intentional self-harm, sequela
10	T40.693A	Poisoning by other narcotics, assault, initial encounter
10	T40.693D	Poisoning by other narcotics, assault, subsequent encounter
10	T40.693S	Poisoning by other narcotics, assault, sequela
10	T40.694A	Poisoning by other narcotics, undetermined, initial encounter
10	T40.694D	Poisoning by other narcotics, undetermined, subsequent encounter
10	T40.694S	Poisoning by other narcotics, undetermined, sequela
10	T40.695A	Adverse effect of other narcotics, initial encounter
10	T40.695D	Adverse effect of other narcotics, subsequent encounter
10	T40.695S	Adverse effect of other narcotics, sequela
10	Z79.891	Long term (current) use of opiate analgesic

Appendix A.2.2 Marginal effect of proportion of providers exposed to academic detailing at different levels of implementation strength for Model 1.



The average proportion of providers exposed to academic detailing was 0.14 (min: 0, max: 0.94).

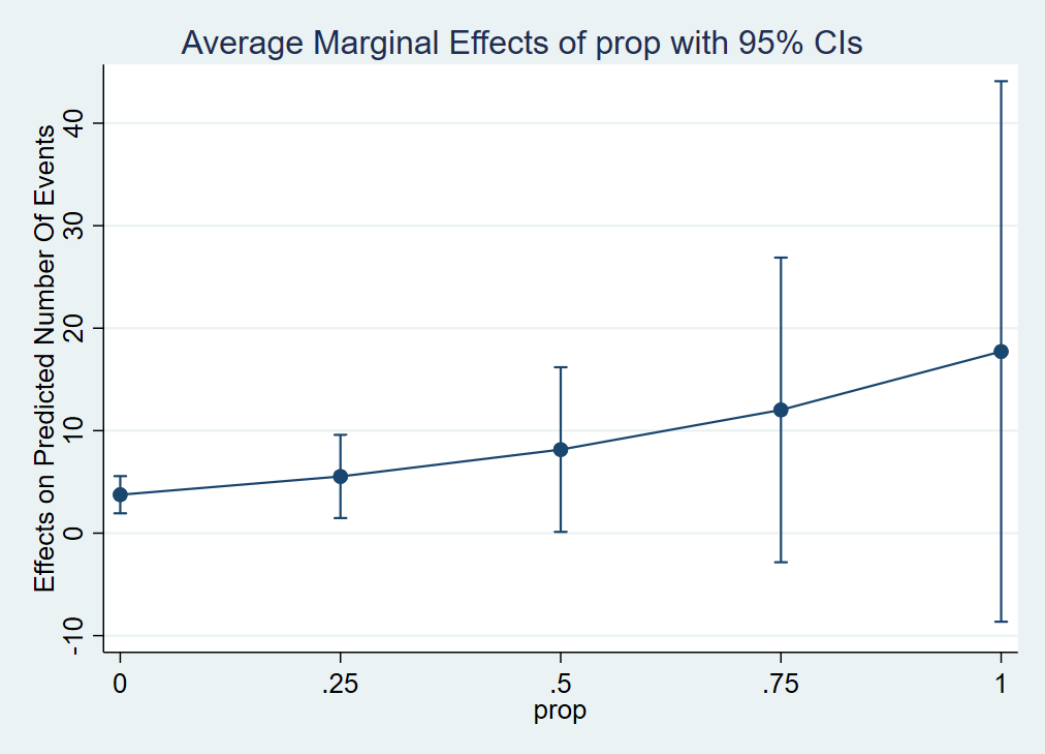
We estimated the mean total number of naloxone prescriptions prescribed by taking the numerical derivative of the expected total monthly naloxone prescriptions prescribed with respect to the proportion of each station:

$$\partial E[Y|\boldsymbol{X}] \,/\, \partial prop = e^{\boldsymbol{\beta X}} * \beta_1.$$

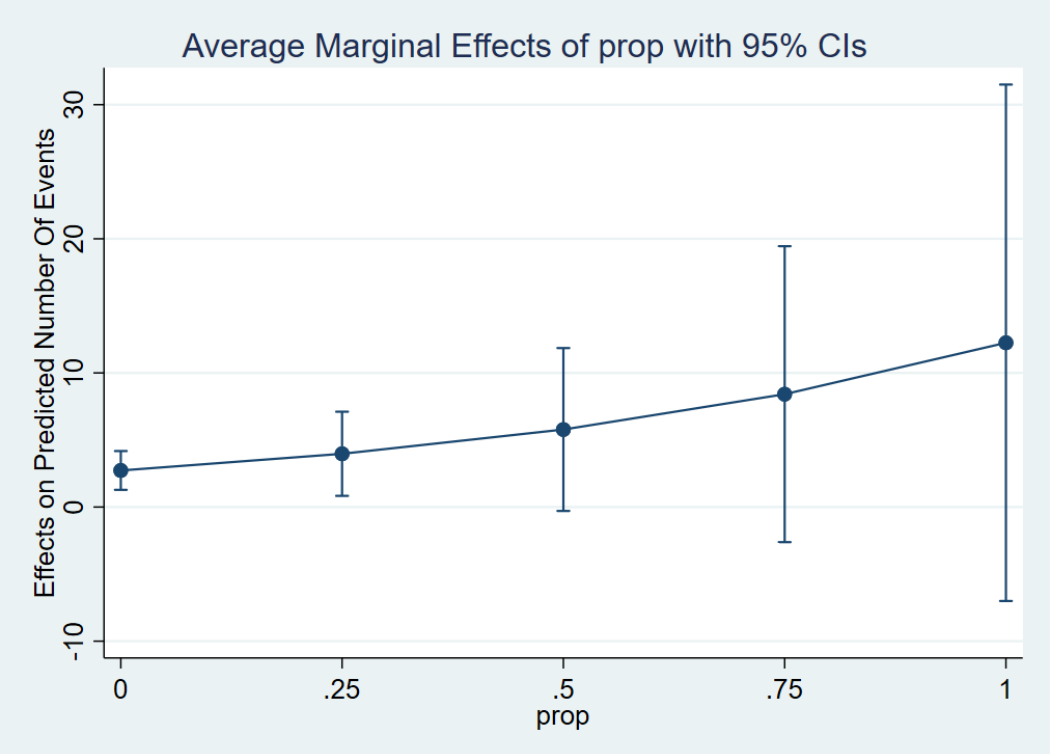
The marginal effect of increasing the proportion from 0% to 100% was a 9.13 increase in the number of naloxone prescriptions prescribed.

As the proportion of providers exposed to OEND-specific academic detailing (`prop`) increases, the effect of the `prop` also changes and in a positive direction.

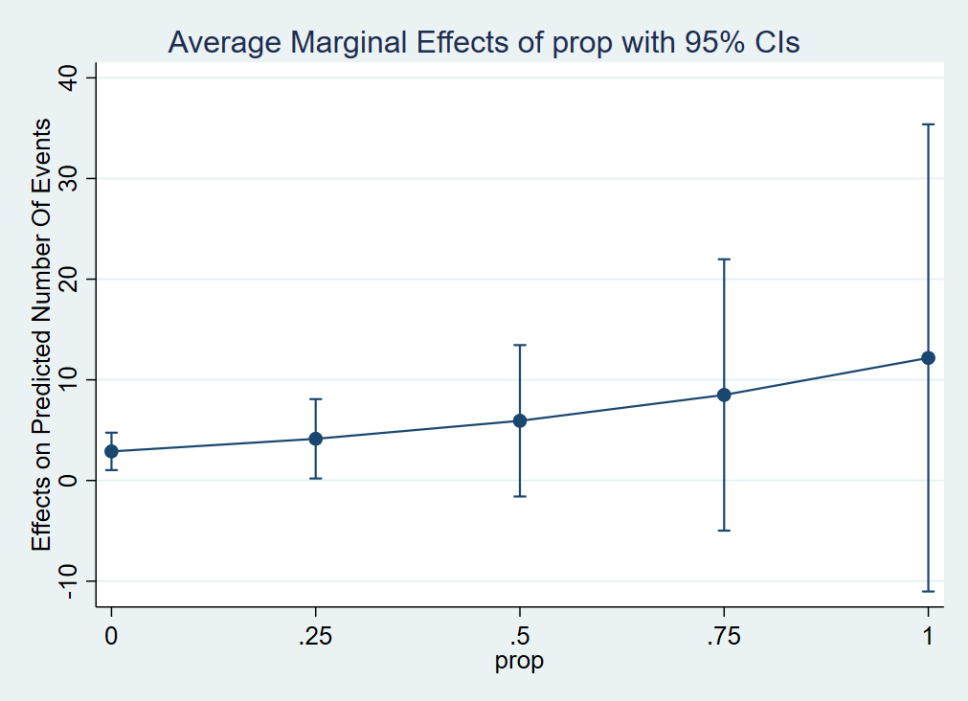
Appendix A.2.3. Marginal effect of proportion of providers exposed to academic detailing at different levels of implementation strength for Model 2 (high risk patients).



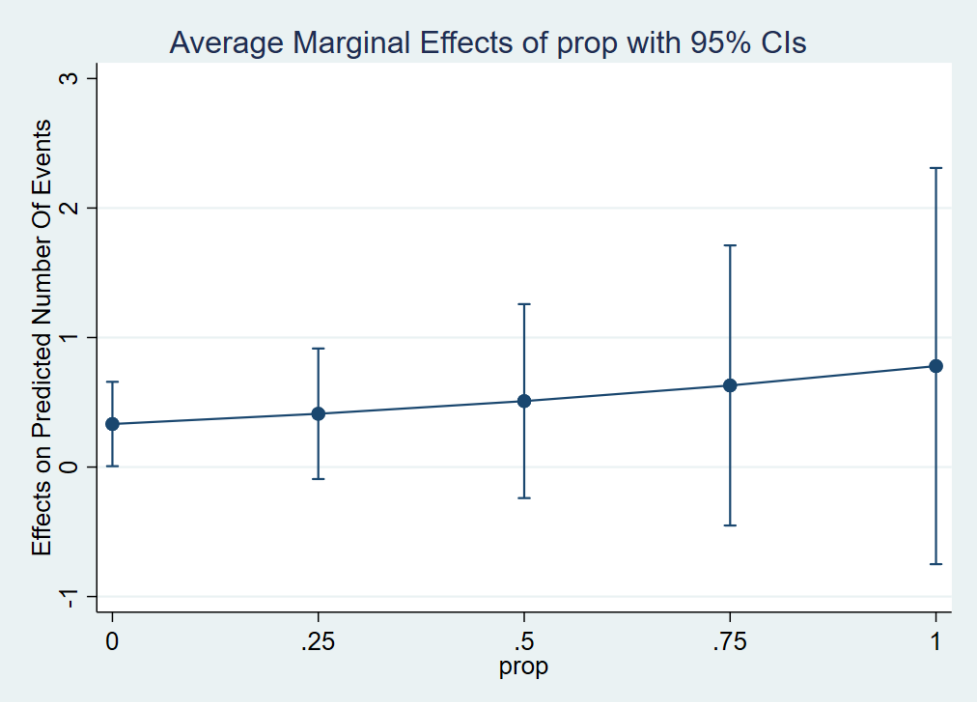
Appendix A.2.4. Marginal effect of proportion of providers exposed to academic detailing at different levels of implementation strength for Model 3 (MEDD >= 50).



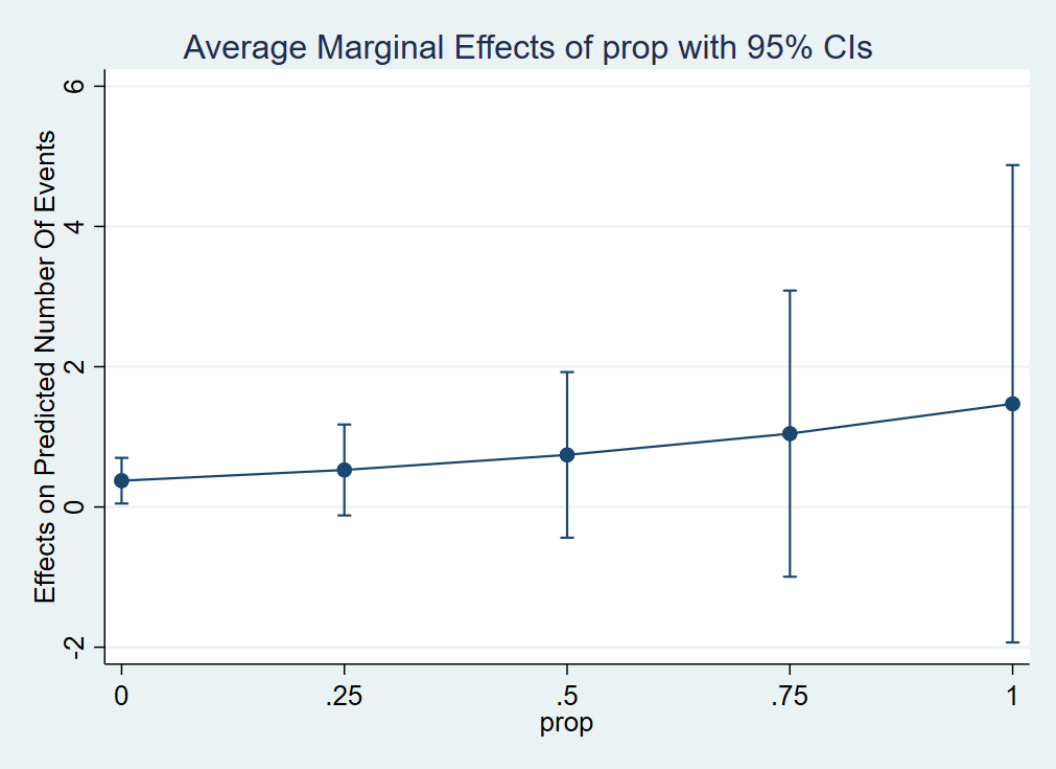
Appendix A.2.5. Marginal effect of proportion of providers exposed to academic detailing at different levels of implementation strength for Model 4 (RIOSORD class >= 5).



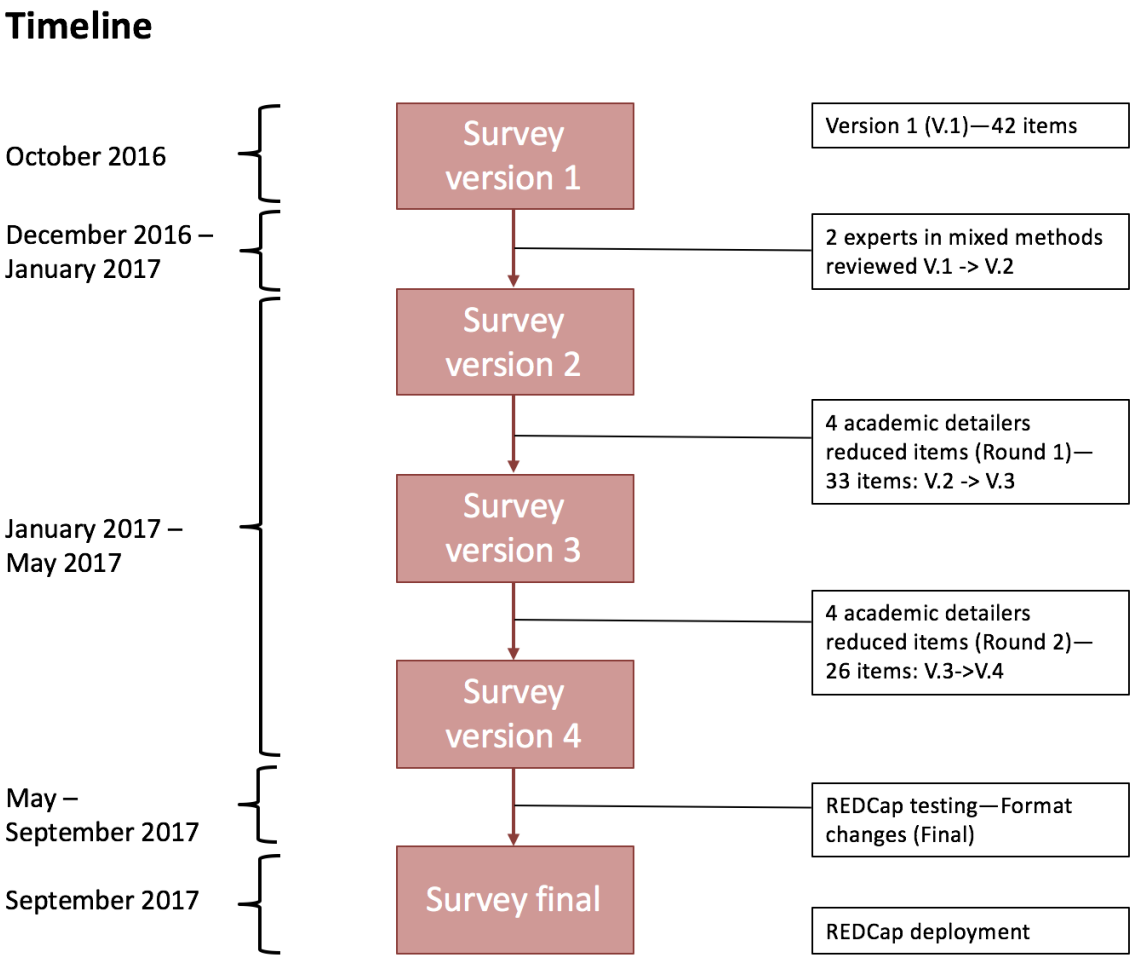
Appendix A.2.6. Marginal effect of proportion of providers exposed to academic detailing at different levels of implementation strength for Model 5 (OUD).



Appendix A.2.7. Marginal effect of proportion of providers exposed to academic detailing at different levels of implementation strength for Model 5 (methadone).



Appendix A.3.1. Flow diagram of survey development, review, and item reduction.



Appendix A.3.2. Final version of the online survey.

Appendix A.3.3. Interview script.

S3. Semi-structured interview and topics.

Topic area	Question/Statement
Knowledge (Concepts and theory about academic detailing)	• As a provider, can you tell me what you know about academic detailing?
Knowledge (changes): Increased knowledge	• What did you learn from the academic detailer?
Professionalism: Relationships / rapport	• Describe your relationship with the academic detailer.
Professionalism: Listening ability	• Do you feel that the academic detailer listens to your needs/issues?
Social norms: Culture	• Describe the culture of naloxone prescribing at your clinic.
Attitude toward writing for naloxone	• How, if at all, has your attitude to using naloxone changed as a result of academic detailing?
Delivery by non-physicians	• How do you feel about having medical education provided by a non-physician?
Implementation: Format (face-to-face)	• Which format is most effective? F2F? Or virtual? • Which do you prefer, face to face vs calls?
Changing behavior (naloxone prescribing	• Do you feel that academic detailing changed the way you prescribe naloxone?
Barriers	• Do you feel that there are barriers to prescribing naloxone?
Facilitators: Academic detailer usefulness	• In what ways would you say the academic detailer helped you.
Educational materials	• What would you say detracted you from understanding the material shared by the academic detailer? Specific elements? • Were the handout materials helpful during the academic detailing visit?
Dashboards	• Do you know what an online clinical dashboard is? Tell me your thoughts. • Have you used the online clinical dashboards?

	• How did the Academic Detailer you met with discuss the online clinical dashboard with you during your meeting?
Repeat visit	• Have you received a repeat visit? • Do you believe a repeat visit is useful?
Leadership	• Does leadership support academic detailing? Tell me about your local leaderships' support and role regarding academic detailing.
Expansion opportunities	• Where do you see academic detailing expanding into next?
Improvement opportunities	• Do you have suggestions for improving the academic detailing service?

Appendix A.3.4. Summary of logistic regressions performed.

The structural form of the logistic regression model was

$$logit(E[Y_i|X_i, W_i]) = logit(p_i) = \ln\left(\frac{p_i}{1-p_i}\right) = \beta_0 + \beta_1 X_i + \delta_{ki}\mathbf{W_{ki}} + \varepsilon_i,$$

where Y_i denotes the outcome (self-stated change in naloxone prescribing) for the *i*-th subject, X_i denotes the main predictor of interest (improved knowledge, improved attitude, and average domain scores), $\mathbf{W_{ki}}$ is a vector that denotes the *k*-number of provider-level covariates, and p_i denotes the probability of the outcome. Baseline characteristics included work history, previous naloxone prescribing, primary care provider status, and previous naloxone-related training.

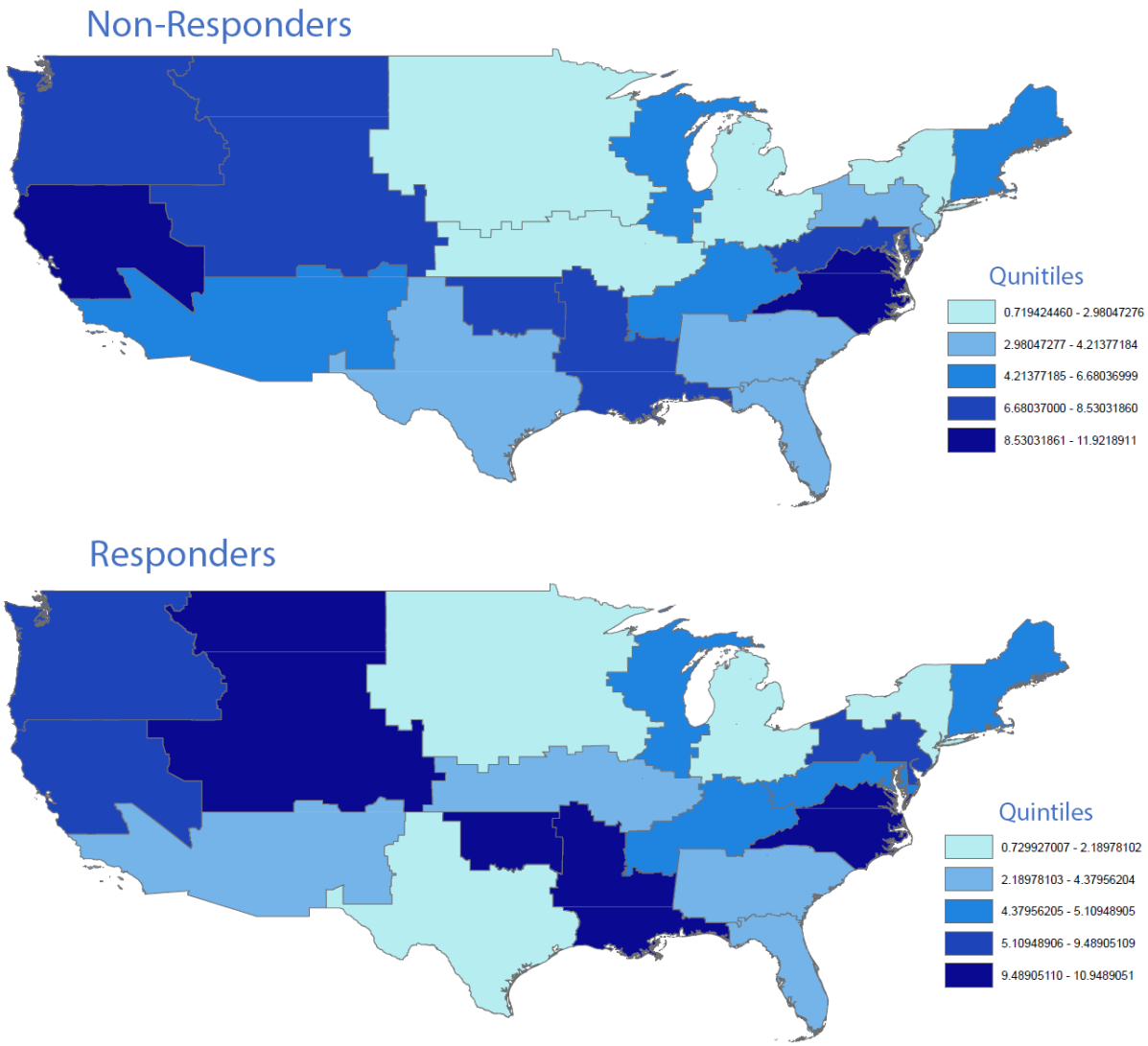
Appendix A.3.5. Comparisons between nonresponders and responders.

Table S5. Comparison between non-responders and responders.

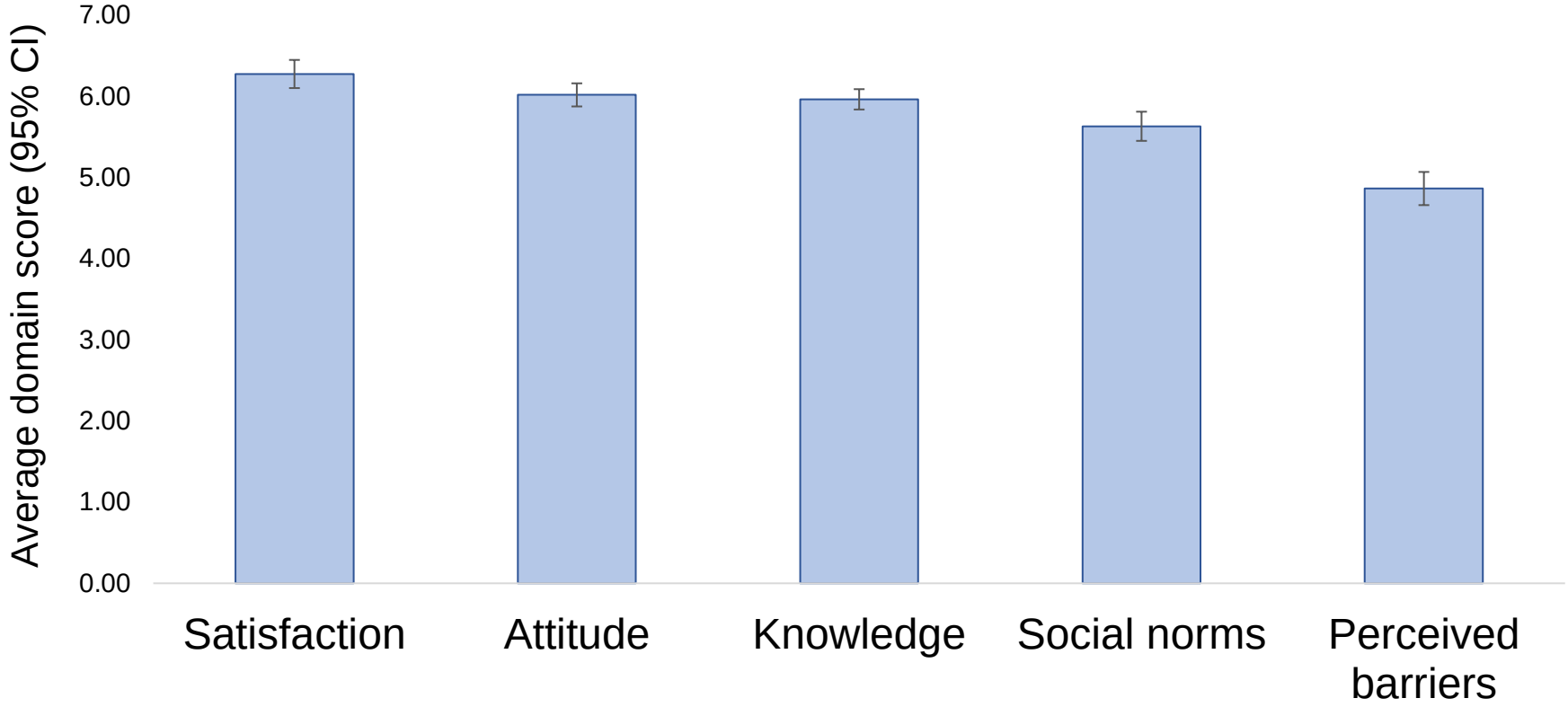
Variable	N	Responders (N=137)	N	Non-responders (N=973)	test statistics	p-value
Age, mean (SD)	101	47 (12)	710	50 (12)	2.26	0.026
Female, n (%)	91	64 (70%)	353	382 (52%)	10.90	0.001
Number of patients, mean (SD)	132	375 (290)	944	413 (315)	1.39	0.165
Number of visits, mean (SD)	60	943 (1060)	459	753 (567)	-1.37	0.176

SD, standard deviation

Appendix A.3.6. Geographic distribution in quintiles of nonresponders and responders at the VA Integrated System.



Appendix A.3.7. Average domain scores for the entire sample (1=Strongly disagree to 7=Strongly agree)

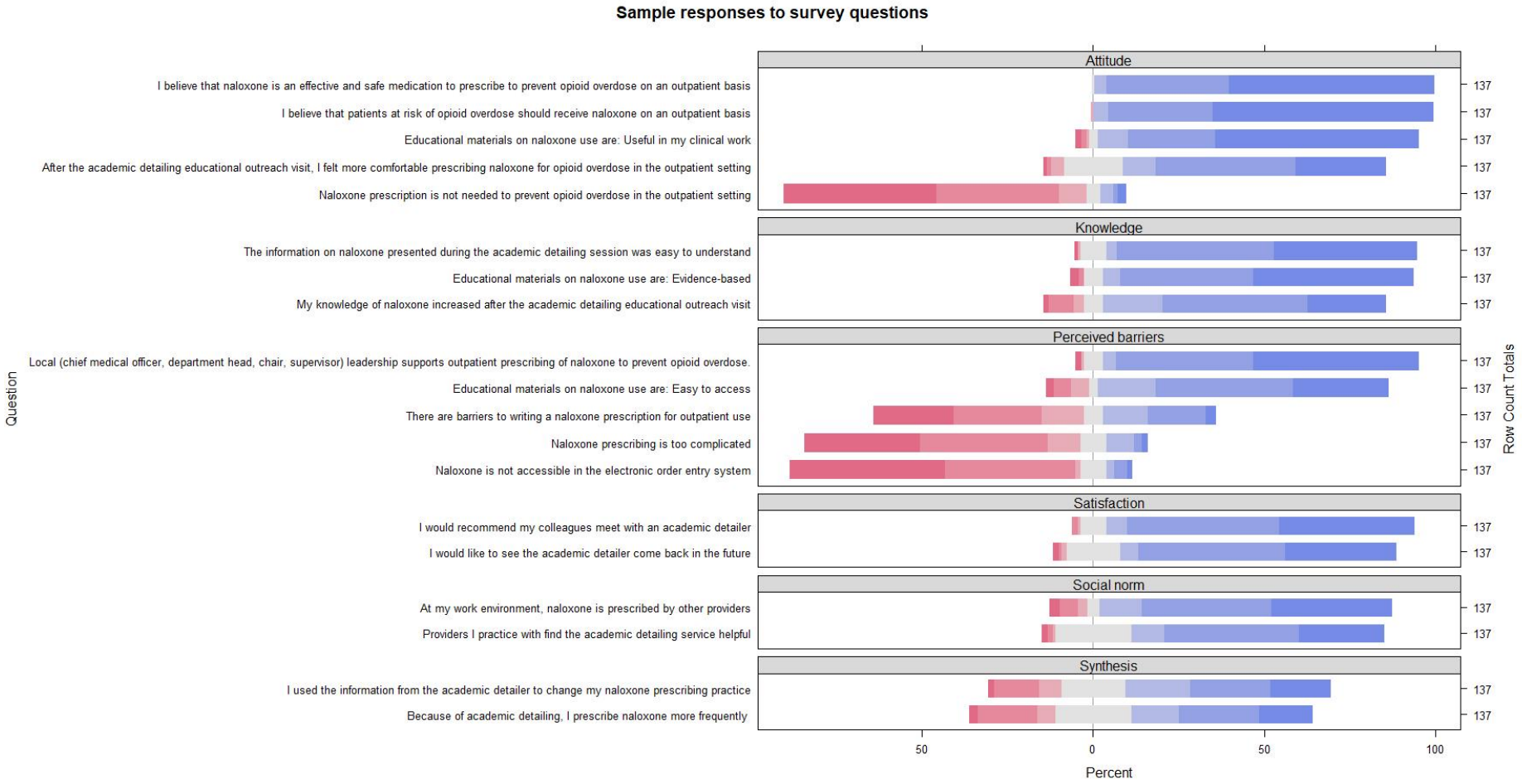


CI, confidence interval

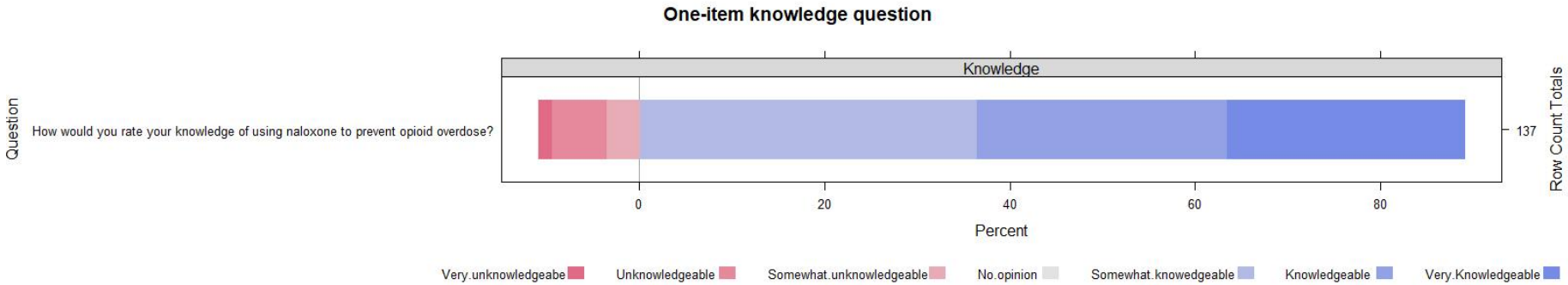
Appendix A.3.8. Average domain scores across different provider types.

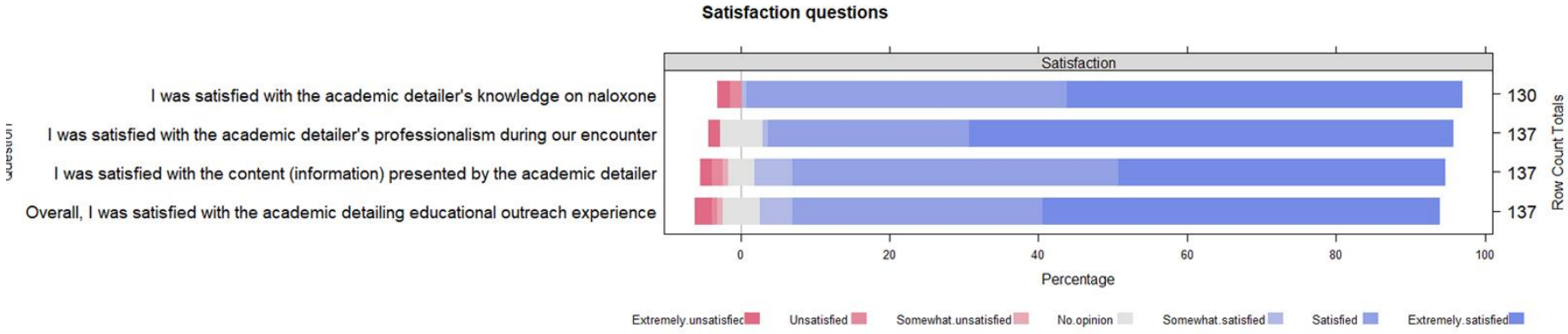
	Total (N=137)		Primary care (N=70)		Specialists (N=29)		Others (N=38)			
Domain	Mean	SD	Mean	SD	Mean	SD	Mean	SD	F stat	p-value
Satisfaction	6.28	1.03	6.13	1.21	6.34	0.95	6.51	0.66	1.76	0.177
Attitude	6.02	0.85	5.86	0.79	6.41	0.75	6.19	0.95	4.62	0.011
Knowledge	5.96	0.75	5.90	0.73	6.11	0.79	5.97	0.74	0.89	0.413
Social norms	5.63	1.07	5.54	1.04	5.90	0.92	5.61	1.22	1.18	0.311
Perceived barriers	4.86	1.22	4.64	1.11	5.46	1.25	4.83	1.27	4.85	0.009

Appendix A.3.9. Descriptive summary of all items on the online survey.*



* We used reverse coding for negative statements.


One-item knowledge question
Knowledge
Question
How would you rate your knowledge of using naloxone to prevent opioid overdose?
137
Row Count Totals
0
20
40
60
80
Percent
Very.unknowledgeabe
Unknowledgeable
Somewhat.unknowledgeable
No.opinion
Somewhat.knowedgeable
Knowledgeable
Very.Knowledgeable


Satisfaction questions
Satisfaction
I was satisfied with the academic detailer's knowledge on naloxone
I was satisfied with the academic detailer's professionalism during our encounter
I was satisfied with the content (information) presented by the academic detailer
Overall, I was satisfied with the academic detailing educational outreach experience
130
137
137
137
Row Count Totals
0
20
40
60
80
100
Percentage
Extremely.unsatisfied
Unsatisfied
Somewhat.unsatisfied
No.opinion
Somewhat.satisfied
Satisfied
Extremely.satisfied

VITA

Mark Bounthavong is a fifth-year PhD candidate in The Comparative Health Outcomes, Policy, and Economics (CHOICE) Institute at the University of Washington. Prior to enrolling at UW, Mark received his Pharm.D. from the College of Pharmacy at Western University of Health Sciences and his MPH from the Rollins School of Public Health at Emory University. Mark's research interests include pharmacoeconomics, outcomes research, health economics, implementation and program evaluations, econometric application, and evidence synthesis using Bayesian methods. Mark also works as the Pharmacy Data Program Manager for the Veterans Health Administration Pharmacy Benefits Management National Academic Detailing Service where he has performed several program evaluations on the National Academic Detailing Service and its impact on the Opioid Overdose Education and Naloxone Distribution (OEND) Program, the Opioid Safety Initiative, and the Psychotropic Drug Safety Initiative.

Mark's CV can be accessed on his website: www.mbounthavong.com