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Impact of Implementing an Academic Detailing Program on Opioid-Benzodiazepine Co-Prescribing Trends at the U.S. Department of Veterans Affairs

Mark Bounthavong, PharmD, PhD,*,†,‡,§ Marcos K. Lau, PharmD, MS, BCPS,* Chad L. Kay, PharmD, BCPS,* Daina L. Wells, PharmD, MBA, BCPS, BCPP,* Sarah J. Popish, PharmD, BCPS, BCPP,* Michael A. Harvey, PharmD, BCPS,* Julianne E. Himstreet, PharmD, BCPS, BCPP,* Andrea Grana, JD, MPH,* Blake A. Freeman, MPP, MBA,* Christina M. Morillo, BPA,* and Melissa L.D. Christopher, PharmD*

*U.S. Department of Veterans Affairs (VA) Pharmacy Benefits Management (PBM) Academic Detailing Service, Washington, District of Columbia, USA; †U.S. Department of Veterans Affairs (VA) Health Economics Resource Center, Menlo Park, California, USA; ‡U.S. Department of Veterans Affairs (VA) Center for Innovation to Implementation, Menlo Park, California, USA; and §Division of Clinical Pharmacy, University of California San Diego, Skaggs School of Pharmacy & Pharmaceutical Sciences, La Jolla, California, USA

Correspondence to: Mark Bounthavong, PharmD, PhD, U.S. Department of Veterans Affairs (VA) Pharmacy Benefits Management (PBM) Academic Detailing Service, 795 Willow Road (152MPD), Building 324 Room D-155, Menlo Park, CA 94025, USA. Tel: 650-709-5627; Fax: 650-617-2639; E-mail: Mark.Bounthavong@va.gov.

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Abstract

Objectives. To assess the process and outcomes of academic detailing to enhance the Opioid Safety Initiative and the Psychotropic Drug Safety Initiative to reduce co-prescribing of opioid-benzodiazepine combinations in veterans. **Methods.** A retrospective cohort design was conducted to evaluate the impact of implementing an academic detailing program on opioid-benzodiazepine co-prescribing between October 2014 through March 2019 at the U.S. Department of Veterans Affairs (VA). The primary outcome was the monthly prevalence of veterans (number per 1,000 population) who were co-prescribed opioid-benzodiazepine combination. Process measure was evaluated using implementation reach (proportion of providers who received academic detailing). Station-level analysis was performed using a linear fixed effects regression model to evaluate the rate of change in the prevalence of veterans co-prescribed opioid-benzodiazepine. **Results.** Altogether 130 VA stations was included for analysis; 119 stations implemented opioid-related or benzodiazepine-related academic detailing, and 11 stations did not. Stations that had implemented academic detailing had a 33% greater monthly reduction on the opioid-benzodiazepine co-prescribing prevalence compared to stations that did not implement academic detailing ($P = .036$). In the linear fixed effects regression model, stations that were expected to have 100% of providers exposed to academic detailing were statistically associated with a greater decrease in the monthly prevalence of Veterans co-prescribed opioid-benzodiazepine by 4.9 veterans per 1,000 population ($P < .001$) compared to stations with 0% of providers exposed to academic detailing. **Conclusions.** Stations that implemented academic detailing and had a higher proportion of providers who were exposed to opioid- or benzodiazepine-related academic detailing had a significant decrease in the monthly prevalence of Veterans co-prescribed opioid-benzodiazepine combinations.

Key Words: Academic Detailing; Implementation Reach; Opioids; Benzodiazepines; Veterans

Background

The United States (U.S.) is in the midst of an opioid epidemic that has consumed the lives of over 47,000 Americans in 2017 [1]. In the general population, over 30% of prescription opioid-related overdose deaths have been associated with a benzodiazepine [2, 3], a class of sedative hypnotics that can lead to unintentional overdose and death [4, 5]. This combination has important implications in the veteran population who have twice the mortality risk for any drug-related overdose death compared to the general U.S. population [6]. Previous studies have reported between 15.9% and 32.0% of veterans were co-prescribed an opioid and benzodiazepine placing them at high risk for an opioid overdose death [7–9].

To address this, Veterans Affairs (VA) launched two national, system-wide campaigns to address the safety and risks associated with opioid and benzodiazepine prescribing in 2013. VA implemented the Opioid Safety Initiative to address opioid overuse by reducing opioid prescribing and expanding access to alternative nonopioid therapies [10]. Additionally, in 2013, the Psychotropic Drug Safety Initiative was implemented to address harmful benzodiazepine prescribing in veterans who were elderly or diagnosed with posttraumatic stress disorder (PTSD) [11]. These two initiatives partnered with the VA Pharmacy Benefits Management (PBM) Academic Detailing Service to help disseminate their key messages using academic detailing. Academic detailers provided key messages that specifically informed providers about the risk of overdose associated with opioid-benzodiazepine co-prescribing. Additionally, academic detailers also delivered key messages on safe opioid and benzodiazepine taper strategies, education of patients on signs and symptoms of withdrawal, incorporation of psychosocial support (e.g., cognitive behavioral therapy), and connecting patients with a substance use disorder clinic to provide opioid use disorder services.

Academic detailing is an educational outreach delivered by specially trained clinicians (also known as academic detailers) to frontline providers with the goal of aligning their practice with current evidence [12–15]. Academic detailing draws on the principles of social marketing [16–18], theory of planned behavior [19], and diffusion of innovation framework [20] to augment providers' prescribing behavior and enhancing health care. Academic detailing consists primarily of face-to-face interactions between the academic detailer and provider where a needs assessment is performed, barrier resolution strategies are developed, balanced evidence and online benchmarking tools are shared, and key messages are delivered to promote voluntary changes in practice behavior to be aligned with current evidence-based practice. Previous studies have reported that academic detailing resulted in improvements to providers' decision-making capabilities that are aligned with evidence-based practice [12, 21]. At VA, academic detailing is primarily delivered by clinical pharmacy specialists who were trained on these principles. Since its implementation, VA academic detailers have made major contributions to reducing inappropriate benzodiazepine prescribing in the elderly [22] and PTSD population [23], increasing naloxone in veterans at risk for opioid overdose [24, 25], and increasing medication-assisted treatment for alcohol use disorder [26].

The PBM Academic Detailing Service, through their partnerships with the Opioid Safety Initiative and the Psychotropic Drug Safety Initiative, has implemented a campaign to reach out to VA providers with patients on either opioids, benzodiazepines, or both to improve prescribing practices associated with this unsafe combination. However, the implementation process of academic detailing may influence its effectiveness; poor implementation may result in a program's failure, while successful implementation may contribute to its success [27, 28]. In our previous study, we reported that increased implementation reach of academic detailing was significantly associated with increased take-home naloxone prescribing rates for opioid overdose events, which highlights the influence of implementation process on a program's outcomes [25]. Therefore, it was critical that we investigate both the effectiveness and implementation process of academic detailing and their impact on opioid-benzodiazepine co-prescribing rates.

The purpose of this quality improvement project was to assess the process and outcomes of academic detailing to enhance the Opioid Safety Initiative and the Psychotropic Drug Safety Initiative in their goal to reduce co-prescribing of opioid and benzodiazepine in the Veteran population.

Methods

Design

A retrospective cohort design was used to evaluate the impact of academic detailing's implementation reach at the station level on the prevalence of opioid-benzodiazepine co-prescribing at VA from October 1, 2014 to March 31, 2019 (54 months). Given that this was a quality improvement project, it was critical that we measure the impact of the program's implementation. The proportion of providers exposed to academic detailing was considered an important process measure to reflect the impact of the program's implementation reach. We previously used this method to address the impact of academic detailing implementation reach on prescribing outcomes at VA [25]. We followed the guidelines set by the Standards for Quality Improvement Reporting Excellence for this quality improvement project [29]. The study protocol was reviewed and given an exemption status as a quality improvement project by the Institutional

Review Boards at Stanford University and the VA Palo Alto Healthcare System.

Setting

This evaluation was performed at VA, the largest, integrated healthcare system in the United States and its territories, which is composed of 170 medical centers and 1,074 outpatient clinics nested within 130 stations [30]. There are 130 instances of the Veterans Information Systems and Technology Architecture (VistA) that incorporates data from all VA stations. For the purpose of this analysis, we will consider each VistA instance a station [31]. Each station contains at least one medical center and several satellite outpatient clinics. VA has an enrollment of over 9 million Veterans and has recorded over 109 million outpatient visits, over 650 thousand inpatient admissions, and 149 thousand inpatient mental health patients treated in fiscal year 2017 [32].

Data Source

Station-, provider-, and patient-level data were accessed using the VA Corporate Data Warehouse, the enterprise data warehouse that stores pharmacy, outpatient, inpatient, and staff data [33]. Provider-level data on receipt of an academic detailing visit for either an opioid-related or benzodiazepine-related outreach visit were captured using Salesforce.com, an online, cloud-based platform designed for customer relationship management, data management, and documentation.

Sample

Provider-level data were used to generate station-level characteristics. All providers, regardless of specialty, were included if they wrote a prescription for an opioid, benzodiazepine, or both. A closed cohort of providers who had active service at VA between October 1, 2014, and March 31, 2019, was used to reduce bias; therefore, providers who left or entered the VA system during the time period were excluded.

Patient-level data included whether they had drug supply on hand within the month determined by the prescribed day supply for an opioid, benzodiazepine, or both. Since the outcome (number of opioid-benzodiazepine prescriptions) would be impacted by short-term use of opioids and benzodiazepine, we opted to exclude any opioid or benzodiazepine prescription that was less than a 5-day supply. Opioid-benzodiazepine co-prescribing was defined as any overlap by day supply within that month. See Supplementary Appendix A1 for the list of eligible opioids and benzodiazepines.

Dependent Variable

Since this analysis was performed at the station level, the outcome of interest was the station-level monthly prevalence of opioid-benzodiazepine co-prescriptions defined as the average monthly number of patients co-prescribed an opioid and benzodiazepine per 1,000 population. The denominator included veterans who were written any prescription in that month.

Independent Variables

VA stations were categorized as implemented or not implemented based on whether an opioid- or benzodiazepine-related visit was performed. We used this categorization to compare the opioid-benzodiazepine co-prescribing rate between VA stations that implemented or did not implement academic detailing during the study time period.

We measured implementation reach by using the proportion of providers who received at least one opioid- or benzodiazepine-related academic detailing outreach at each station. We categorized providers as exposed when they first received academic detailing for any opioid-related key message associated with the Opioid Safety Initiative or any benzodiazepine-related key message associated with the Psychotropic Drug Safety Initiative; providers who did not receive an academic detailing visit were considered unexposed. A closed cohort of providers was used to fix the denominator for each station to reduce confounding associated with providers entering or leaving VA during the study period.

Additional variables included the provider's age, gender, years worked at VA, and district (regional) location at the station level. Data on the number of outpatient visits, inpatient visits, emergency department/urgent care visits, number of unique patients receiving a prescription, and the number of academic detailers at each station were also included as time-varying station-level characteristics.

Statistical Analyses

Descriptive analysis was used to characterize the stations; information on the average monthly number of outpatient visits, inpatient discharges, emergency department/urgent care visits, and outpatient prescriptions written for unique patients were provided. Additionally, station-level information about providers included their average age, proportion of males, length of employment (years) at the beginning of the study period, and their assigned districts. Baseline characteristics were compared between stations that implemented academic detailing and did not implement academic detailing using independent t tests for continuous data and chi square tests for discrete data.

Comparisons between Stations That Implemented and Did Not Implement Academic Detailing

Differences in the station-level average monthly prevalence rates of veterans co-prescribed an opioid and benzodiazepine were compared between stations that implemented and did not implement opioid- or benzodiazepine-related academic detailing programs

Table 1. Characteristics of providers who prescribed an opioid or benzodiazepine at the Veterans Health Administration

Variables	All Providers N = 17,704	Providers at VA stations that implemented academic detailing (N = 16,842)	Providers at VA stations that did not implement academic detailing (N = 862)	*P*-value	Missing data
Age (years), mean (SD)	49.2 (3.1)	49.1 (3.1)	50.0 (2.3)	<.001	0 (0.0%)
Gender, n (%)					
Male	7,881 (55.1%)	7,481 (55.2%)	400 (54.6%)	.752	3,410 (19.3%)
Female	6,413 (44.9%)	6,080 (44.8%)	333 (45.4%)		
Years worked at VA, n (%)					
Less than 1 year	2,451 (15.5%)	2,341 (15.6%)	110 (13.7%)	.047	1,867 (10.6%)
1 to < 5 years	3,750 (23.7%)	3,562 (23.7%)	188 (23.4%)		
5 to < 10 years	3,915 (24.7%)	3,702 (24.6%)	213 (26.5%)		
10 to < 15 years	2,452 (15.5%)	2,306 (15.4%)	146 (18.2%)		
15 to < 20 years	1,337 (8.4%)	1,265 (8.4%)	72 (9.0%)		
20 to < 25 years	979 (6.2%)	941 (6.3%)	38 (4.7%)		
>25 years	953 (6.0%)	916 (6.1%)	37 (4.6%)		
District, n (%)					
North Atlantic	4,410 (24.9%)	4,190 (24.9%)	220 (25.5%)	<.001	0 (0.0%)
Southeast	3,385 (19.1%)	3,385 (20.1%)	0 (0.0%)		
Midwest	3,596 (20.3%)	3,131 (18.6%)	465 (53.9%)		
Continental	2,860 (16.2%)	2,860 (17.0%)	0 (0.0%)		
Pacific	3,453 (19.5%)	3,276 (20.1%)	177 (20.5%)		

SD = standard deviation.

using a linear form of the generalized estimating equation model with identity link and autoregressive correlation controlling for station-level characteristics such as the mean age of providers, mean number of years providers worked at VA, proportion of male providers, monthly number of outpatient visits, the monthly number of inpatient discharges, the monthly number of emergency department/urgent care visits, the monthly number of patients receiving a prescription, the monthly number of academic detailers, the proportion of pain specialists, proportion of primary care providers, and proportion of mental health providers. Clustered standard errors were estimated to account for repeated measures at the station level. Results were presented as the adjusted monthly prevalence rate along with the corresponding 95% confidence interval (CI).

Impact of Implementation Reach on Opioid-Benzodiazepine Co-Prescribing Rates

Additionally, panel data analysis was performed to evaluate the change in the station-level average monthly prevalence rate due to the change in the proportion of providers who received academic detailing using a linear fixed effects regression model. Since the unit of analysis was the station, the fixed effects model adjusted for station-level time-varying covariates such as the monthly number of outpatient visits, the monthly number of inpatient discharges, the monthly number of emergency department/urgent care visits, the monthly number of patients receiving a prescription, and the monthly number of academic detailers. Clustered standard errors were estimated to account for repeated measures at the station level. Results were presented as the adjusted monthly prevalence rate along with the corresponding 95% CI. Hausman specification test was performed to confirm the appropriateness of using a fixed effects model [34, 35].

Statistical significance was defined as a two-tailed alpha less than 0.05. All statistical analyses were performed using Stata MP Version 15 (Stata Corp., College Station, TX).

Results

A total of 130 stations comprising 17,706 providers were included for analysis; 119 stations implemented opioid-related or benzodiazepine-related academic detailing, and 11 stations did not. The average age of providers was 49.2 (SD 3.1) years; most were male (55.2%) and worked for VA for 5 to <10 years (24.7%) (Table 1). There were more providers located in the North Atlantic district (24.9%) followed by the Midwest (20.3%), Pacific (19.5%), Southeast (19.1%), and Continental (16.2%) districts. A total of 16,842 providers (95.1%) were part of stations that implemented academic detailing compared to 862 providers (4.9%) who were part of VA stations that did not. Providers at stations that implemented academic detailing were significantly younger (49.1 vs 50.0 years, $P < .001$), had a larger proportion of providers working at VA for 5 years or less (39.3% vs 37.1%, $P = .047$), and had more providers in the

Table 2. Baseline characteristics of VA stations (N = 130) that implemented and did not implement academic detailing

Variable	All VA stations (N = 130)	VA stations that implemented academic detailing (N = 119)	VA stations that did not implement academic detailing (N = 11)	*P*-value*
Prevalence† of pain specialists, mean (SD)	7.90 (0.01)	7.91 (0.01)	7.76 (0.01)	.967
Prevalence† of primary care providers, mean (SD)	266 (0.08)	260 (0.07)	332 (0.10)	.044
Prevalence† of mental health providers, mean (SD)	141 (0.05)	142 (0.06)	134 (0.04)	.617
Monthly number of unique outpatient visits, mean (SD)	22,837 (13,139)	23,386 (13,073)	16,899 (12,959)	.139
Monthly number of unique inpatient visits, mean (SD)	439 (336)	545 (339)	283 (254)	.058
Monthly number of unique emergency department/urgent care visits, mean (SD)	1,345 (872)	1,392 (881)	843 (574)	.012
Monthly number of unique pharmacy patients, mean (SD)	14,531 (8,291)	14,910 (8,270)	10,430 (7,707)	.091
Monthly number of unique academic detailers, mean (SD)	0.1 (0.4)	0.11 (0.45)	0.00 (0.00)	.009
Division, n (%)				
North Atlantic	36 (27.7%)	32 (26.9%)	4 (36.4%)	.184
Southeast	20 (15.4%)	20 (16.8%)	0 (0.0%)	
Midwest	27 (20.8%)	23 (19.3%)	4 (36.4%)	
Continental	23 (17.7%)	23 (19.3%)	0 (0.0%)	
Pacific	24 (18.5%)	21 (17.7%)	3 (27.3%)	

*Number per 1,000 providers.
†*P* values represent the comparison between stations that implemented academic detailing to stations that did not implement academic detailing.
SD = standard deviation.

Southeast and Continental districts (31.1 vs 0.0%, $P < .001$). The average duration of an opioid- or benzodiazepine-specific academic detailing visit was 28.8 minutes (SD 22.2) and the average number of visits during the study time period was 3.3 visits (SD 4.3).

At baseline, the average station had approximately 22,837 (SD 13,139) outpatients visits, 439 (SD 336) inpatient admissions, 1,345 (SD, 872) emergency department/urgent care department visits, and 14,531 (SD 8,291) unique patients with at least one prescription issued per month (Table 2). At baseline, VA stations that had implemented academic detailing had more academic detailers compared to stations that did not implement academic detailing (0.11 vs 0.0, $P = .009$). Additionally, stations that did not implement academic detailing had a higher prevalence of primary care providers compared to station that did (332 vs 260 per 1,000 providers, $P = .044$). There were no other significant differences in baseline characteristics between stations that implemented and did not implement academic detailing.

There was a lot of variation in the proportion of providers who received academic detailing across the stations suggesting that academic detailing implementation was not uniform or consistent (see Supplementary Appendix A2). Of 130 stations that were assessed, 11 (8.5%) stations did not have a provider receive academic detailing associated with any opioid- or benzodiazepine-related outreach during the study period. The average proportion of providers per station that received academic detailing outreach for either opioid- or benzodiazepine-related outreach was 25.5% (range: 0.0% to 75.0%). Figure 1 illustrates the station-level average proportion of providers who received academic detailing and the station-level prevalence of Veterans receiving an opioid-benzodiazepine combination across the study time period.

Implemented versus Non-Implemented Stations

At baseline, the prevalence of patients on opioid-benzodiazepine combination was similar between stations that implemented academic detailing and did not implement academic detailing (29.2 vs 25.9 per 1,000 population; $P = .289$). However, stations that had implemented academic detailing had a greater reduction in the average monthly prevalence rate of patients on opioid-benzodiazepine combination compared to stations that did not implement academic detailing throughout the study time period (−0.44 vs −0.33 opioid-benzodiazepine combinations per 1,000 population, $P < .036$). In other words, stations that had implemented academic detailing had a 33% greater monthly reduction in opioid-benzodiazepine co-prescribing compared to stations that have not implemented academic detailing. Figure 2 illustrates the differences in prevalence rates between stations that implemented and did not implement academic detailing for the study period.

Impact of Implementation Reach on Opioid-Benzodiazepine Co-Prescribing Rates

In the fixed effects model, stations with an expected increase in the proportion of providers who received an academic detailing visit from 0% to 100% were statistically significantly associated with a decrease in the monthly prevalence of veterans co-prescribed opioid-benzodiazepine combination by 4.9 patients per 1,000 population ($P < .001$) controlling for potential confounders.

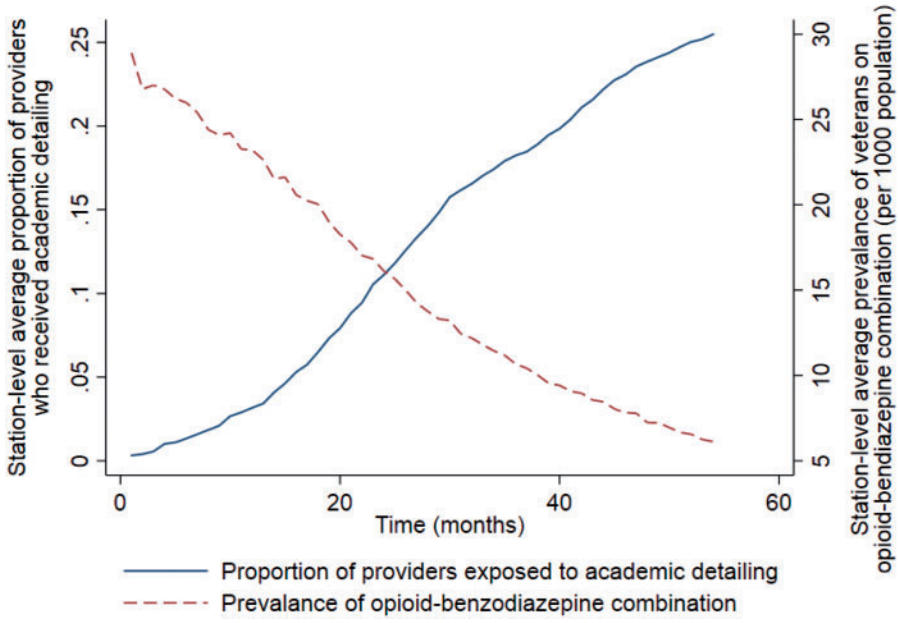

Figure 1. Average station-level proportion of providers who received academic detailing and station-level prevalence of veterans receiving an opioid-benzodiazepine combination at the Veterans Health Administration, October 1, 2014, to March 31, 2019. The proportion of providers who received opioid- or benzodiazepine-related academic detailing visit increased during the study period. During the same period, the prevalence of opioid-benzodiazepine combinations decreased.

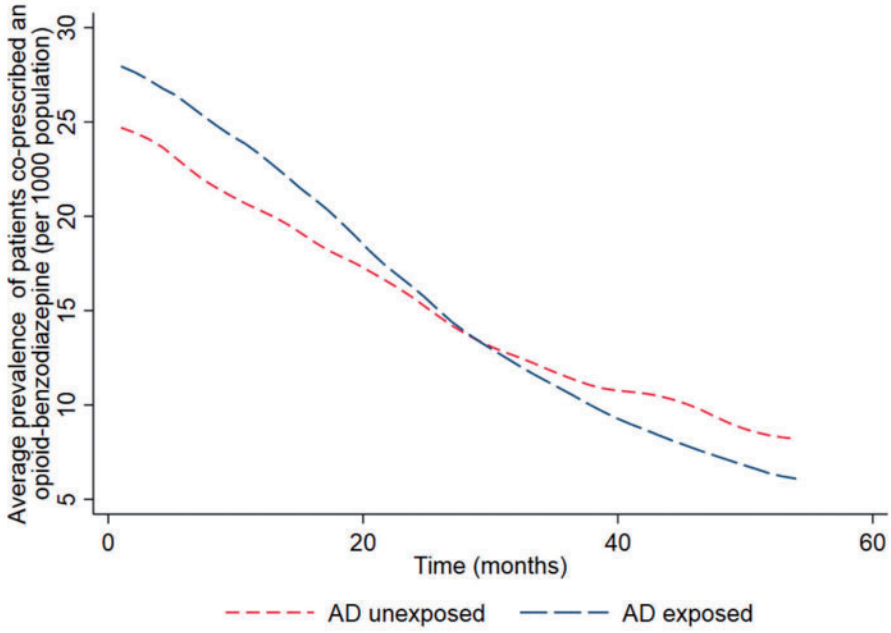

Figure 2. Co-prescribed opioid-benzodiazepine prevalence trends of stations that implemented academic detailing, October 1, 2014, to March 31, 2019. VA stations that implemented opioid- or benzodiazepine-related academic detailing programs (AD exposed) had a greater reduction in the prevalence of opioid-benzodiazepine combinations compared to VA stations that did not implement these programs (AD unexposed) during the study period ($P = .036$).

In other words, if a hypothetical station had 100% of its providers exposed to academic detailing, then they will have a monthly reduction of 4.9 patients with an opioid-benzodiazepine combination per 1,000 population compared to a station that had 0% of its providers exposed to academic detailing.

Discussion

In this quality improvement project, stations with providers who were exposed to opioid- or benzodiazepine-related educational outreach had significant decreases in the average monthly prevalence of Veterans

co-prescribed an opioid-benzodiazepine regimen between October 1, 2014, and March 31, 2019. Additionally, stations that had a greater proportion of providers who received academic detailing had a greater rate of reducing unsafe co-prescribing of an opioid-benzodiazepine combination. However, none of the stations had 100% of their providers receive academic detailing; the average was 25.5% (range: 0.0% to 75.0%), which indicates that continued investment on implementation reach is needed in order to maximize the benefits.

It is important to note that during the study period the Opioid Safety Initiative and Psychotropic Drug Safety Initiative were on-going. We expected to see reductions in the prevalence of opioid-benzodiazepine co-prescribing but were interested in the differences in the rate of reduction. Hence, we used time as a fixed effect to account for secular changes due to other unmeasured confounders. In our analysis we reported reductions in the prevalence of opioid-benzodiazepine combinations at both stations that did and did not implement academic detailing. Among stations that implemented academic detailing, there were greater reductions, which suggest that academic detailing enhanced the benefits associated with these national initiatives. Additionally, increasing the number of providers who received academic detailing has the potential to diffuse the information at their VA station. It is unclear how much diffusion added to the overall effectiveness of academic detailing but using the proportion of providers who received academic detailing as a process measure provides us with some indication of its influence.

In this quality improvement project, we opted to focus on discontinuation of either an opioid or benzodiazepine as our outcome measure; this has several advantages. First, providers do not necessarily write for both opioids and benzodiazepines for their patients. Many patients receive their opioid and benzodiazepine prescriptions from different providers. Therefore, discontinuing one of these agents would remove the risk associated with opioid-benzodiazepine co-prescribing. It should be noted that patients could have their medications slowly tapered, which could reduce the risk, but we did not evaluate this in our analysis. Second, providers do not need to receive academic detailing for both the Opioid Safety Initiative and Psychotropic Drug Safety Initiative to eliminate the risk associated with opioid-benzodiazepine co-prescribing. As long as the provider changes their prescribing behavior for one of the agents, risk is mitigated. Finally, academic detailers can flexibly target opioid risk, benzodiazepine risks, or the risk of the combination based on providers' needs.

Stations that implemented opioid-related or benzodiazepine-related academic detailing had higher numbers of monthly outpatient, inpatient, and emergency department/urgent care visits, more prescription fills and more primary care providers than stations that did not. Although these were controlled for in our regression models, the differences between the groups cannot be ignored and could potentially yield other factors that were not considered in this study. Further exploration as to the cause of these differences may reveal insights that would benefit program managers and decision makers.

Our study adds to the growing literature on academic detailing's impact on promoting evidence-based treatment, particularly with opioids and benzodiazepines. Previous studies have reported that academic detailing augments provider's benzodiazepine prescribing to be aligned with the current evidence-based practice. Ragan and colleagues reported that VA providers, after receiving an academic detailing outreach visit, had a greater reduction in the monthly prevalence of elderly patients receiving harmful benzodiazepine prescriptions compared to before the intervention (monthly difference of 0.42 per 1,000 veterans, $P < .01$) [22]. A separate study reported that VA providers who received academic detailing had a greater reduction in the monthly prevalence of inappropriate benzodiazepine prescribing in patients diagnosed with PTSD compared to providers who did not receive academic detailing (a monthly difference of 1.30 per 1,000 veterans, $P = .002$) [23]. Compared to these previous studies, the difference in opioid-benzodiazepine reduction between stations that implemented and did not implement academic detailing was lower (a monthly differences of 0.11 per 1,000 veterans). This suggests that the clinical significance may not be as large as previous reports; hence, it is necessary to translate this into direct clinical end points such as overdose events or mortality. Future studies will need to establish the relationship between academic detailing implementation and direct clinical end points.

Despite our best efforts, there are several limitations to our design that deserve discussion. First, we opted to perform a station-level analysis instead of a provider-level analysis because of the challenges associated with different providers writing for either an opioid, benzodiazepine, or both. By evaluating academic detailing's impact at the station level, we were able to associate the proportion of providers who received academic detailing to the prevalence of opioid-benzodiazepine co-prescribing. This strategy is not uncommon and has been presented before as a valid method to associate academic detailing reach with prescribing changes [25, 26]. Another benefit of this measurement is that it provides us with an important process measure to reflect academic detailing's implementation reach, which is an important element of program success.

Second, our study did not evaluate the number of providers who wrote for both opioids and benzodiazepines for their patients. These providers may be different from other providers who prescribe one or the other and may require additional attention by the academic detailer such as increased duration of the educational outreach or additional visits. Due to the challenges of identifying

when an academic detailing interaction was a follow-up for either the opioid- or benzodiazepine-related educational outreach visit, we were unable to determine whether academic detailing was effective in providers who wrote for both opioids and benzodiazepines compared to others who only prescribed for one or the other. Additionally, we were unable to measure the dose reduction of either an opioid or benzodiazepine prescription as a possible outcome. With the release of the U.S. Food and Drug Administration Drug Safety Communication on the harm associated with sudden discontinuation of an opioid prescription [36], it is recommended that providers and patients opt for careful dose reduction rather than abrupt discontinuation.

Next, the Veterans Health Administration and Department of Defense released updated guidelines on pain management and benzodiazepine in 2017, which may have caused secular changes in the prevalence of patients co-prescribed an opioid-benzodiazepine [37]. Moreover, other VA programs were also implemented during this time period that focused on reducing opioid-benzodiazepine prescribing such as the introduction of prior authorization consults [38] and chart review notes [39]. To account for this, we performed an analysis comparing the opioid-benzodiazepine co-prescribing rates between stations that implemented and did not implement academic detailing, and we used panel data analysis with a fixed effects model to address any secular changes by adding a variable for time in months in our regression models and controlling for station-level time-varying covariates [34, 35].

Another limitation is the heterogeneity between stations in terms of implementation reach. None of the stations achieved 100% exposure for their providers; the maximum was 75%. Sites may have high (or low) intensity of reaching providers at the beginning or later in the study period. Moreover, sites may have unmeasured confounders that could influence how much academic detailing is provided, which would confound the analysis. To account for this, we used a fixed effects model, which handles the omitted variable bias problem [34, 35]. As long as the relevant time-varying confounders were captured in the model, we reduce the bias associated with time-invariant confounders. By using sites as fixed effects, they act as their own control over time resulting in an interpretation that any changes in outcome is associated with the changes in the proportion of providers exposed to academic detailing within that site.

Since these findings were generated in a Veteran population, our findings may not be generalizable to other healthcare systems. However, we believe that large, integrated healthcare systems similar to VA will benefit from these findings and use them to help inform whether or not to implement academic detailing at their institutions. Additionally, we focused on veterans who received prescriptions from VA only; hence, our findings may not be generalizable to those veterans who acquire prescriptions outside VA. Furthermore, we used a closed cohort of providers in our evaluation which limits our ability to make conclusions about new providers and providers who left VA during the study period.

Conclusion

Academic detailing has an important role in reducing harmful opioid-benzodiazepine co-prescribing. Increasing the proportion of providers receiving opioid- or benzodiazepine-related academic detailing outreach reduces the prevalence of harmful opioid-benzodiazepine co-prescribing. This investigation highlights the importance of implementation reach on academic detailing's effectiveness at reducing harmful opioid-benzodiazepine co-prescribing and may be an important metric for future implementation planning.

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Supplementary Data

Supplementary data are available at *Pain Medicine* online.

References

1. National Institute on Drug Abuse. Overdose Death Rates. 2019. Available at: https://www.drugabuse.gov/related-topics/trends-statistics/overdose-death-rates (accessed June 2019).
2. Tori ME, Larochelle MR, Naimi TS. Alcohol or benzodiazepine co-involvement with opioid overdose deaths in the United States, 1999–2017. JAMA Netw Open 2020;3(4):e202361.
3. Wilson N. Drug and opioid-involved overdose deaths—United States, 2017–2018. MMWR Morb Mortal Wkly Rep 2020;69 (11):290–7. doi: 10.15585/mmwr.mm6911a4.
4. Sieghart W. Pharmacology of benzodiazepine receptors: An update. J Psychiatry Neurosci 1994;19(1):24–9.
5. Rudolph U, Crestani F, Benke D, et al. Benzodiazepine actions mediated by specific gamma-aminobutyric acid(A) receptor subtypes. Nature 1999;401(6755):796–800.
6. Bohnert AB, Valenstein M, Bair MJ, et al. Association between opioid prescribing patterns and opioid overdose-related deaths. JAMA 2011;305(13):1315–21.

7. Bernardy NC, Lund BC, Alexander B, Friedman MJ. Increased polysedative use in veterans with posttraumatic stress disorder. Pain Med Malden Mass 2014;15(7):1083–90.
8. Morasco BJ, Duckart JP, Carr TP, Deyo RA, Dobscha SK. Clinical characteristics of veterans prescribed high doses of opioid medications for chronic non-cancer pain. Pain 2010;151 (3):625–32.
9. Carico R, Zhao X, Thorpe CT, et al. Receipt of overlapping opioid and benzodiazepine prescriptions among veterans dually enrolled in Medicare part D and the Department of Veterans Affairs: A cross-sectional study. Ann Intern Med 2018;169 (9):593–601.
10. Gellad WF, Good CB, Shulkin DJ. Addressing the opioid epidemic in the United States: lessons from the Department of Veterans Affairs. JAMA Intern Med 2017;177(5):611–2.
11. Wiechers IR. Improving psychopharmacological care for older veterans: implementation of phase 2 of the psychotropic drug safety initiative. Am J Geriatr Psychiatry 2016;24(3):S155–6.
12. Avorn J, Soumerai SB. Improving drug-therapy decisions through educational outreach: A randomized controlled trial of academically based "detailing." N Engl J Med 1983;308 (24):1457–63.
13. Wells DL, Popish S, Kay C, Torrise V, Christopher ML. VA academic detailing service: Implementation and lessons learned. Fed Pract 2016;33(5):66–9.
14. Popish SJ. Academic detailing: Using clinical evidence to improve care. Ment Health Clin 2013;2(12):392–4.
15. Farhadian S, Yee MV, Christopher MLD. Fostering the use of clozapine in the severely mentally ill through academic detailing. Ment Health Clin 2011;1(5):94–8.
16. Evans WD. How social marketing works in health care. Br Med J 2006;332(7551):1207–10.
17. Evans WD, McCormack L. Applying social marketing in health care: Communicating evidence to change consumer behavior. Med Decis Making 2008;28(5):781–92.
18. Grier S, Bryant CA. Social marketing in public health. Annu Rev Public Health 2005;26(1):319–39.
19. Ajzen I. The theory of planned behavior. Organ Behav Hum Decis Process 1991;50(2):179–211.
20. Rogers EM. Diffusion of Innovation, 4th edition. New York, NY: The Free Press; 1995.
21. Avorn J, Soumerai SB, Everitt DE, et al. A randomized trial of a program to reduce the use of psychoactive drugs in nursing homes. N Engl J Med 1992;327(3):168–73. doi: 10.1056/NEJM199207163270306
22. Ragan AP, Aikens GB, Bounthavong M, Brittain K, Mirk A. Academic detailing to reduce sedative-hypnotic prescribing in older veterans. J Pharm Pract 2019. Online ahead of print. doi: 10.1177/0897190019870949.
23. Bounthavong M, Lau MK, Popish SJ, et al. Impact of academic detailing on benzodiazepine use among veterans with posttraumatic stress disorder. Subst Abuse 2020; 41 (1): 101–9. doi: 10.1080/08897077.2019.1573777.
24. Bounthavong M, Harvey MA, Wells DL, et al. Trends in naloxone prescriptions prescribed after implementation of a National Academic Detailing Service in the Veterans Health Administration: A preliminary analysis. J Am Pharm Assoc 2017;57(2):S68–72.
25. Bounthavong M, Devine EB, Christopher MLD, Harvey MA, Veenstra DL, Basu A. Implementation evaluation of academic detailing on naloxone prescribing trends at the United States Veterans Health Administration. Health Serv Res 2019;54 (5):1055–64.
26. Harris AHS, Bowe T, Hagedorn H, et al. Multifaceted academic detailing program to increase pharmacotherapy for alcohol use disorder: Interrupted time series evaluation of effectiveness. Addict Sci Clin Pract 2016;11(1):15.
27. Durlak JA. Why program implementation is important. J Prev Interv Community 1998;17(2):5–18.
28. Durlak JA, DuPre EP. Implementation matters: A review of research on the influence of implementation on program outcomes and the factors affecting implementation. Am J Community Psychol 2008;41(3–4):327–50.
29. Ogrinc G, Mooney SE, Estrada C, et al. The SQUIRE (Standards for QUality Improvement Reporting Excellence) guidelines for quality improvement reporting: Explanation and elaboration. BMJ Qual Saf 2008;17(Suppl 1):i13–32.
30. U.S. Department of Veterans Affairs. VHA Vitals. Washington, DC: Department of Veterans Affairs; 2020.
31. Evans DC, Nichol WP, Perlin JB. Effect of the implementation of an enterprise-wide Electronic Health Record on productivity in the Veterans Health Administration. Health Econ Policy Law 2006;1(2):163–9.
32. U.S. Department of Veterans Affairs. *Veterans Health Administration Fiscal Year 2017 Annual Report: Modernizing Veteran Health Care*. Washington, DC: U.S. Department of Veterans Affairs; 2018.
33. U.S. Department of Veterans Affairs. *172VA10P2: VHA Corporate Data Warehouse – VA. 79 FR 4377*. Washington, DC: Department of Veterans Affairs; 2014.
34. Hilbe JM. Negative Binomial Regression, 2nd edition. Cambridge: Cambridge University Press; 2013.
35. Allison PD. Fixed Effects Regression Models, 1st edition. Newbury Park, CA: SAGE Publications, Inc.; 2009.
36. U.S. Food and Drug Administration. FDA identifies harm reported from sudden discontinuation of opioid pain medicines and requires label changes to guide prescribers on gradual, individualized tapering. *FDA*. 2019. Available at: http://www.fda.gov/drugs/fda-drug-safety-podcasts/fda-identifies-harm-reported-sudden-discontinuation-opioid-pain-medicines-and-requires-label-changes (accessed November 2019).
37. Department of Veterans Affairs and Department of Defense. *VA/DoD Clinical Practice Guideline for the Management of Posttraumatic Stress Disorder and Acute Stress Disorder.* Washington, DC: Department of Veterans Affairs and Department of Defense; 2017. Available at: https://www.healthquality.va.gov/guidelines/MH/ptsd/VADoDPTSDCPGFinal082917.pdf (accessed December 2017).
38. Pardo D, Miller L, Chiulli D. Implementation of a pharmacy consult to reduce co-prescribing of opioids and benzodiazepines in a veteran population. Subst Abuse 2017;38(2):157–60.
39. Shayegani R, Pugh MJ, Kazanis W, Wilkening GL. Reducing coprescriptions of benzodiazepines and opioids in a veteran population. Am J Manag Care 2018;24(8):e265–9.