Trends & Trajectories of Prescription Opioids in the Military Health System

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FINAL REPORT

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Trends & Trajectories of Prescription Opioids in the Military Health System

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14. ABSTRACT-
Background: Opioid analgesics are the most misused drug class in the United States, second only to marijuana. Misuse and abuse by military service members is now an urgent concern. Increased use of opioids to treat chronic pain appears to be related to increased opioid misuse and abuse. The 2009 Department of Defense (DoD) Survey of Health Related Behaviors among Active Duty Military Personnel revealed substantial increases in misuse of prescription drugs, attributed overwhelmingly to opioid analgesics. Both overall DoD and Army rates were significantly higher than the civilian rate of prescription drug misuse during the same period. To address similar problems with opioid misuse and abuse, states have initiated electronic prescription monitoring programs (PMP) that track all scheduled medications from pharmacies within the state. **Objective**: The objective of the project is to utilize PMP technology and innovations to develop and test an opioid-related misuse prevention intervention using surveillance and detection to support clinical care in military settings. We will include standardized population level and individual-user level reports and guidelines to inform utilization of PMP data. This will support future efforts to develop further intervention activities; for example, the development of provider and patient educational activities and brief interventions similar to those that have been developed by state PMPs. **Study Design**: We will use a combination of quantitative and qualitative methods to: (1) develop and test prescription database search algorithms (similar to those used in state PMPs) for identifying potential opioid misuse within the military setting; (2) generate and evaluate standardized reports and guidance documents in preparation for implementing a 'provider-focused' query and reporting system appropriate to the military context; and (3) develop a final set of intervention recommendations suitable for implementation the DOD Military Health System. Quantitative data will be extracted from the DoD Prescription Drug Tracking System (PDTS) and linked with linked patient data from the Military Health System (MHS) Data Repository (MDR).

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1.0 EXECUTIVE SUMMARY

Opioid analgesics are commonly misused and abused in the United States (US). Among military service members, opioid misuse and abuse is now an urgent concern. Increased use of opioids to treat chronic pain appears to be related to increased opioid misuse and abuse. The 2009 Department of Defense (DoD) Survey of Health Related Behaviors among Active Duty Military Personnel revealed substantial increases in misuse of prescription drugs, attributed overwhelmingly to opioid analgesics. Both overall DoD and Army rates were significantly higher than the civilian rate of prescription drug misuse during the same period. To address similar problems with opioid misuse and abuse, states have initiated electronic prescription monitoring programs (PMP) that track all scheduled medications from pharmacies within the state.

2.0 INTRODUCTION

Accompanying this rise in opioid prescriptions is a staggeringly high increase in individuals seeking treatment for opioid addiction and opioid-related deaths. The consequences of opioid misuse include a dramatic increase in opioid-related emergency department visits, poisoning deaths, opioid-related addiction treatment, and suicides.

Unfortunately, the opioid misuse epidemic has not spared the US military. In the Army, oxycodone and hydrocodone are commonly prescribed analgesics. The 2009 DoD Survey of Health Related Behaviors among Active Duty Military Personnel reported a substantial increase in opioid misuse, doubling from 2002-2005 and nearly tripling from 2005-2008. In 2008, 10.1% of active duty military personnel misused opioids in the prior month while 17.2% misused in the preceding 12 months.

Military leadership and the Institute of Medicine committee on substance use disorders in the military identified improving the surveillance and monitoring of opioid prescribing as a military health priority to prevent opioid misuse and reduce opioid-related morbidity and mortality. In response to the opioid misuse and problem in the United States, there is now increased surveillance and monitoring of prescription drug use and misuse across a variety of domains. This includes the advent of federally funded, state implemented drug monitoring program (PMPs). Most PMPs track all controlled substances (Schedules II-V) from all payers dispensed at non-Federal pharmacies within the state. Within the military, a PMP has a variety of potential disease prevention and health promotion applications including as a resource to monitor individual patient prescribing, to conduct military health surveillance and intervention, to allow detection of illicit behaviors, to improve pharmacy practices, and to track medical and nonmedical use of prescriptions to inform policy on prescribing, medication access, racial disparities and other issues. Prescription monitoring is part of a balanced approach ensuring appropriate access to scheduled medications for those who need them while minimizing risk of abuse and addiction.

Implementing an opioid risk mitigation system in the military context is not without challenges. Preliminary research is needed to create intervention materials, evaluate potential barriers and facilitators to implementing the system, and determine the best trial design to test the system. We

conducted preliminary feasibility/proof of concept research of an opioid misuse prevention intervention including the development of provider and patient educational activities and brief interventions similar to those that have been developed by state PMPs that will support clinical care in military settings with their inherent unique challenges.

This work is a mixed-methods project with a quantitative (project 1) and qualitative (project 2) component. This report will address Project 1, the quantitative component.

Aim 1: To develop and test prescription database algorithms, utilizing a model developed and implemented successfully with civilian PMPs, for identifying non-medical use of scheduled medications and/or 'questionable' activity
   a. Adapt algorithms used in civilian PMPs to identify non-medical use of opioids in the military context
   b. Based on Sub-aim A, develop empirical models using both pharmacy and medical claims to predict opioid misuse, substance abuse and dependence, and opioid-related poisonings, and assess the predictive validity of pharmacy claims for surveillance and early warning of opioid related problems.

3.0   METHODS, ASSUMPTIONS AND PROCEDURES

3.1   Aim 1

To develop and test prescription database algorithms, utilizing a model developed and implemented successfully with civilian PMPs, for identifying non-medical use of scheduled medications and/or 'questionable' activity

3.1.1   Sub-aim A. Adapt algorithms used in civilian PMPs to identify non-medical use of opioids in the military context

3.1.2   Sub-aim B. Based on Sub-aim A, develop empirical models using both pharmacy and medical claims to predict opioid misuse, substance abuse and dependence, and opioid-related poisonings, and assess the predictive validity of pharmacy claims for surveillance and early warning of opioid related problems.

3.1.3   Methods. Retrospective statistical analyses were conducted to address sub-aim A and B.

Sub-aim A
After obtaining Institutional Review Board approvals from the San Antonio Military Center and Wilford Hall Ambulatory Surgical Center, we obtained a de-identified dataset derived from the Military Health Systems (MHS) Management Analysis and Reporting Tool (M2). M2 data are derived from electronic health record, pharmacy, and other non-DoD data sources outside of the combat theater to produce validated and quality-controlled metrics of DoD health care worldwide. Data Description Administrative prescription records (Pharmacy Data Transaction Service [PDTS]) were used. The Data Discovery, Analytics, and Research (DDAR) team from the Enterprise Intelligence Section within the Defense Health Agency selected the cohort by identifying activity duty service members (ADSMs) who received at least one opioid

prescription and were continuously enrolled in TRICARE Prime for 11 of 12 months for each year and obtaining M2 data for those individuals.

Procedures

To adapt an algorithms used in civilian PMPs to identify non-medical use of opioids in the military context; all ADSMs receiving at least one opioid prescription between 2008 and 2014 were included in the analysis. A running count was created to provide the number of providers and dispensers for (1) the given month and the previous two months (three months total), (2) for each month, and (3) for any patient that received an opioid prescription in a given month. After the running count was created, a count of unique patients crossing the 5 prescribers x 5 dispensers x 3 month (5x5x3) threshold each year was computed. Alternative existing algorithms, e.g., 10x10x3 and 5x5x6, and exploratory algorithms, based on input from MHS providers and leadership (from Project 2, qualitative), were also implemented. This was to compare PDTS results and explore whether the 5x5x3 is the optimal algorithm for use in the MHS.

To further address sub-aim A, we developed a longitudinal dataset with opioid prescription data from 2006 to 2014 to examine patterns of opioid use in ADSMs. For comparison, publicly available data were gathered from IMS Health to identify prescription patterns in the insured civilian population. Publicly available data were gathered from the DoD Personnel Workforce Reports/Publications, the Congressional Reporting Service, and the Defense Casualty Analysis system to account for population trends in the military that may influence opioid use patterns.

Sub-aim B

After obtaining approval from institutional and DoD regulatory agencies, we obtained a de-identified cohort from the DDAR team within the Enterprise Intelligence Section (EI), part of the Defense Health Agency (DHA). The dataset was derived from the Military Health System Mart (M2) and included pharmacy data from the PDTS, information from the inpatient and outpatient data files. Inpatient and outpatient data extracts from the DDAR team included socio demographic characteristics and yearly comorbidity variables derived using the Johns Hopkins ACG system. These data extracts were merged with pharmacy data using an encrypted patient identifier common to both files. Based on sub-aim A, we assessed factors associated with acute versus 3 long-term opioid use patterns – episodic, long-term low-dose (LT Low), and long-term high-dose (LT High) and identify modifiable factors that may mitigate opioid risk in US ADSMs who received care in the MHS beginning in 2012 or 2013.

Procedures

Opioid episodes were operationalized based on Von Korff, Saunders, & Ray (2008); however, months were used to define opioid episodes rather than days. An opioid episode began the month of the first opioid prescription filled during 2012-2013, and continued until the last month the opioid prescription was dispensed without subsequent opioids fills for 6 months. Only the first opioid episode for each patient was considered for this analysis. Acute episodes were those lasting less than 3 months, and long-term episodes were those spanning 3 months or longer. Long-term episodes were further delineated into episodic, LT LOW, or LT HIGH. Long-term episodes with less than 120 days supply or fewer than 10 fills were defined as episodic. Long-term episodes spanning 120 days or longer, having 10 or more prescription fills, and an average

daily dose less than 20 milligrams morphine equivalent (MME) across the episode, were considered LT LOW. Long-term episodes spanning 120 days or longer, having 10 or more prescription fills, and an average daily dose greater than 20 MME were classified as LT HIGH.

3.1.4 Data Analysis.

Sub-aim A
To adapt an algorithms used in civilian PMPs to identify non-medical use of opioids in the military context we applied the 5x5x3 algorithm to PDTS data for ADSMs of the US Armed Forces. After completing the running count, a count of unique patients crossing the 5x5x3 threshold each year between 2008 and 2014 was computed. Alternative existing algorithms, e.g., 10x10x3 and 5x5x6, and exploratory algorithms, based on input from MHS providers and leadership, were also implemented. This was to compare PDTS results and explore whether the 5x5x3 is the optimal algorithm for use in the MHS.

To determine whether similar patterns of yearly opioid use were observed between ADSM and civilian populations in 2006 to 2014, total opioid prescription counts were compared for both yearly counts and yearly percent change. The total counts were projected on a double-axis plot with proportional scaling to minimize visual ambiguity. The yearly percent changes for both active duty and civilian data were graphed for comparison purposes. We used an autoregressive forecast model to verify changes in opioid use patterns before and after 2011. Several interrupted time series models examined whether military system-level factors were associated with changes in opioid use.

Sub-aim B
To assess opioid episodes, univariate and bivariate statistics were conducted to characterize opioid episode types and compare covariates by episode type. Distributions were tested using Chi square tests for categorical variables and analysis of variance (ANOVA) tests for continuous variables. Multinomial logistic regression analysis was conducted on factors associated with each type of opioid episode (episodic, LT LOW, LT HIGH vs. acute). Analyses were conducted with proc logistic in SAS Enterprise Guide 7.1.

Model variables included: (1) patient demographics: year and sponsor service, sex; age and marital status; (2) patient prior period risk factors: co-occurrence of benzodiazepine and antidepressant, tobacco use diagnosis, substance use diagnosis, and (3) patient covariates: counts of ER visits not resulting in inpatient admission, receipt of a major inpatient procedure (e.g. hysterectomy, knee replacement, pacemaker insertion, etc.), unique provider counts, and diagnoses of musculoskeletal signs and symptoms, acute sprains and strains, fractures excluding digits, cervical pain syndromes, headaches/migraines, head injury, low back pain, and 2nd- and 3rd-degree burns.

4.0   MAJOR EVENTS/MILESTONES/SUCCESS

- Obtained Institutional Review Board (IRB) approval from all intuitions – October 31, 2015

- Created data dictionary, cleaned database, created variable labels and categories for key variables of interest - January 2016
- Standardized opioid prescriptions to morphine milligram equivalent (MME) in database – January 2016
- Conducted retrospective data analysis on demographic variables, patient risk factors (e.g., co-occurring prescription medication and substance use diagnosis), and opioid characteristics (e.g., averaged prescribed MME, averaged day supply) - February 2016 to December 2017
- Created interactive tool to compare project data to other data registries - July 2016
- Manuscript on opioid use patterns submitted to Military Medicine - March 2017 (accepted with revise and resubmit)
- Manuscript accepted to Military Medicine - July 2017
- Oral presentation at 2016 San Antonio Military Health Systems and Universities Research Forum (SURF)
- Symposium at the 2016 SURF
- Oral presentation at 2017 College on Problems of Drug and Dependence (CPDD),
- 4 Poster presentations at 2017 MHSRS
- 2 poster presentations at 2017 SURF
- Poster presentation at 2017 Behavior, Biology, and Chemistry: Translational Research in Addiction (BBC)
- Poster presentation at 2018 CPDD

5.0   RISK ASSESSMENT

5.1   Risk Analysis

Scheduling delays during the project:
- Project start day delayed due to difficulty delivering administrative dataset to the South Texas Veterans Health Care System (STVHCS) because of IRB issues at Wilford Hall and San Antonio Military Health System (SAMHS).
- Proposed milestones were delayed due to significant issues with the administrative dataset and technical documentation during 01 August 2016 to 30 November 2016.
- IRB approval was re-obtained from all institutions for updated administrative dataset.
- In November 2016, we were informed there was a misspecification with prescriber IDs, thus delaying the analysis of Applying Civilian Prescription Drug Monitoring Program (PDMP) Algorithms to Prescription Records from PDTS (5x5x3). See 5.2 Technical Challenges for more information.

5.2   Technical Challenges

While working with the dataset provided to us, three technical issues were found to be problematic with our dataset. These challenges resulted from how the data was delivered from DOD and failure to provide full data with a standard deidentification process. Without these challenges the project would have realized the opportunities available from the data more successfully and with greater impact.

- First, we discovered that the anonymized prescriber and dispenser identifiers had a one to one match. Because of this we were unable to generate counts of dispensers and prescribers, which prevented us from replicating many civilian PDMP metrics in our analysis.
- Second, the data was only for ADSMs and their families that had been active for eleven out of twelve months in a given year. This made selecting a longitudinal difficult and introduced bias into our models.
- Finally, the ACG were found to be problematic for our needs. The substance abuse code provided by the ACG system did not differentiate between different substances which prevented us from making models that specifically examined opioid abuse and watered down the effects in our models. Additionally, we were unable to specifically define what these ACG codes represented other than their high-level definitions.

6.0 TRANSITION PLAN

6.1 Military Relevance

Given the prevalence of chronic pain and opioid misuse in the military, if a novel approach were shown to improve the identification of opioid misuse and substance abuse and dependence, it would positively impact morbidity associated with the opioid misuse in ADSMs. The use of PMPs in the medical setting constitutes as a major improvement to the military and civilian sectors by potentially providing providers with critical information about patients who are at risk for opioid misuse, substance abuse, or substance dependence. The PMPs also relates information about patient's adverse events and provides valuable information to identify non-medical use of scheduled medications and/or 'questionable' activity. Additionally, military research studies on opioid use to date have focused largely on prevalence and associated factors; however, given what is known about the association of risk factors about opioids, PMPs would positively impact both military and civilians providers in identify aberrant drug behaviors. The project demonstrates it is possible to apply PMP strategies; however, it should be noted that a public health framework will be important to avoid unintentional negative downstream consequences on quality of care and career.

6.2 Transition Strategy

The outcome of this work could lead to the advancement of PMPs early identification of opioid misuse, substance abuse and dependence, opioid-related poisoning and identifying pharmacy claims and early warning signs of opioid related problems. Our results demonstrated that aberrant drug taking behaviors and sociodemographic variables (e.g., sex, age) among ADSMs were similar to that of civilians. This knowledge may be incorporated into clinical guidelines for prescribing opioids, PMPs, and complex clinical scenarios, such as results of this study can be extrapolated to healthcare providers who interact with patients experiencing chronic pain. Lastly, our scientific results may guide safe and appropriate use of opioids and inform public policy related to prescription opioid use and abuse.

7.0   RESULTS

Sub-aim A
We investigated which PMP risk threshold (e.g., 5x5x3 or 10x10x3) was the most common across all 50 states within the US. We determined that the most common PMP threshold was the 5x5x3 (B-4). More importantly, the PMP thresholds varied across states and many thresholds were not accessible. Therefore, we utilized the most common PMP threshold, 5x5x3, to compared civilian and ADSMs. See table 1.

Table 1. Prescription Drug Monitor Risk Thresholds Applied by States

Threshold	# of States*	States
5 prescribers and 5 dispensers in 3 months	27	CA, CO, CT, FL, HI, ID, IL, KY, MN, NV, NH, NM, OR, PA, SD, TN, UT, WV, IN, NC, WA, NY, AL, AK, VA, RI, ME
10 prescribers and 10 dispensers in 6 months	4	NC, AL, AK, VA
Other Count of Prescribers or Dispensers	9	ND, LA, MS, AR, OH, KS, IA, MI, MA
Threshold includes Milligram Morphine Equivalent (MME)	2	WA, OH
>1 substance use flag (e.g. benzodiazepine and opioid)	2	WA, ME
No PDMP	1	MO
Unknown Thresholds	11	AZ, DE, GA, MD, MT, NE, NJ, SC, TX, WI, VT

*Includes Washington, DC and states with >1 risk threshold

Between 2008 and 2014, as many as 1,711 or 0.463% (i.e., in 2011) of active duty patients met or exceeded the 5x5x3 threshold within a year. To compare to the civilian population, the Florida PDMP FORSCE, was used. Between October 2011 and December 2011, the rate of active duty patients exceeding the 5x5x3 was 0.26% for TRICARE and 0.08% for FORSCE. In 2012, the rate of patients exceeding the 5x5x3 was 0.44% for TRICARE and 0.18% for FORSCE. See table 2.

Table 2. Florida's 5x5x3 Threshold Compared to PDTS Data

|	PDTS (TRICARE)			Florida PDMP (FORSCE)		
Quarter	Individuals with Opioid Rx	Exceeding 5x5x3	Proportion Exceeding 5x5x3	Individuals with Opioid Rx	Exceeding 5x5x3	Proportion Exceeding 5x5x3
10/2011 -12/2011	109,692	285	0.26%	3,156,182	2381	0.08%
1/2012 - 3/2012	110,174	141	0.13%	3,396,372	2064	0.06%
4/2012 - 6/2012	109,771	156	0.14%	3,226,855	1870	0.06%
7/2012 - 9/2012	107,975	186	0.17%	3,160,011	1799	0.06%

*Tramadol and Schedule 5 Drugs excluded

The next set of results analyzed patterns of yearly opioid use between ADSM and civilian populations in 2006 to 2014 (A-1). Between 2006 and 2014, 1,516,979 ADSM filled 7,119,945 opioid prescriptions in military treatment facilities or purchased through TRICARE. Refills accounted for 3.99% of these prescriptions. Peak opioid fills occurred in August 2011 (84,801 fills) with 4.59% (58,923) of the non-deployed ADSM receiving at least one prescription fill.

Both active duty and civilian populations showed signs of decreasing use after 2011, but this change was much more pronounced among ADSM. See figure 1.
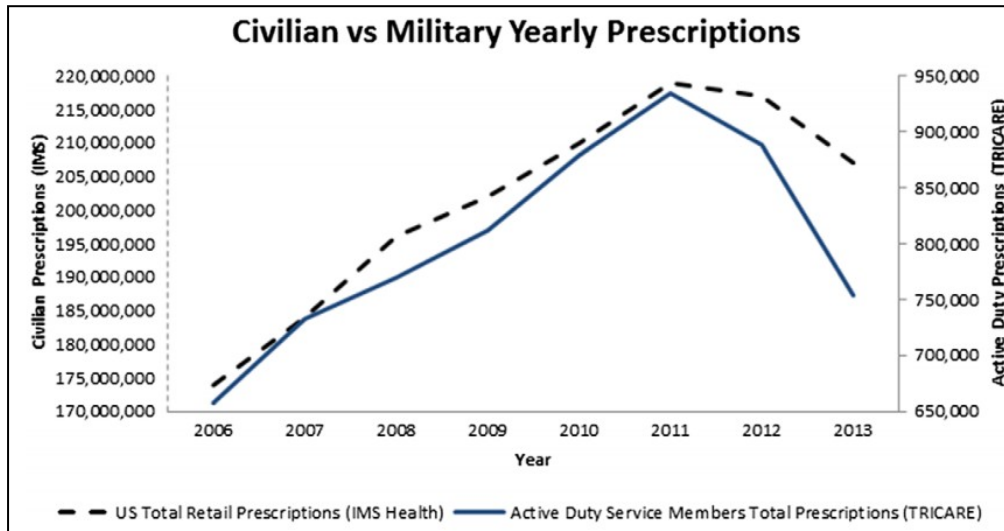

Figure 1. Yearly Prescription Counts from TRICARE (Active Duty Military) and IMS (Civilian Retail) Pharmacies

After 2011, these counts showed signs of decrease in both populations, but much more so among ADSMs. In 2012, opioid prescriptions among ADSMs dropped by 5% compared with 1% in the civilian population; in 2013, they dropped by 15% among ADSMs compared with 5% among civilians. The forecast model showed a significant difference after 2011 between the projected and actual proportion of ADSMs filling an opioid prescription, confirming 2011 as a point of divergence in opioid use. See figure 2.
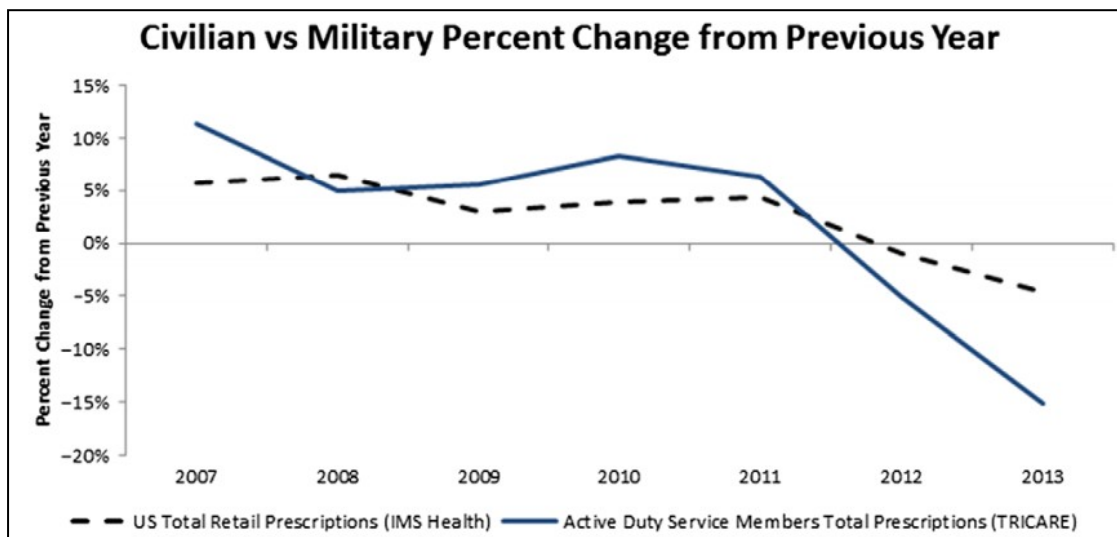
Figure 2. Percent Change From Previous Year for Non-Deployed Active Duty Military and Civilian (IMS) Populations (TRICARE and IMS Databases)

The proportion of ADSMs who filled an opioid prescription declined between 2011 and 2012, between 2012 and 2013, and between 2013 and 2014. Between December 2011 and December 2014, the proportion of ADSMs who filled an opioid prescription dropped below the 95% confidence interval for all but 3 months, meaning there was a significantly lower proportion of ADSMs with an opioid prescription than projected. See figure 3.
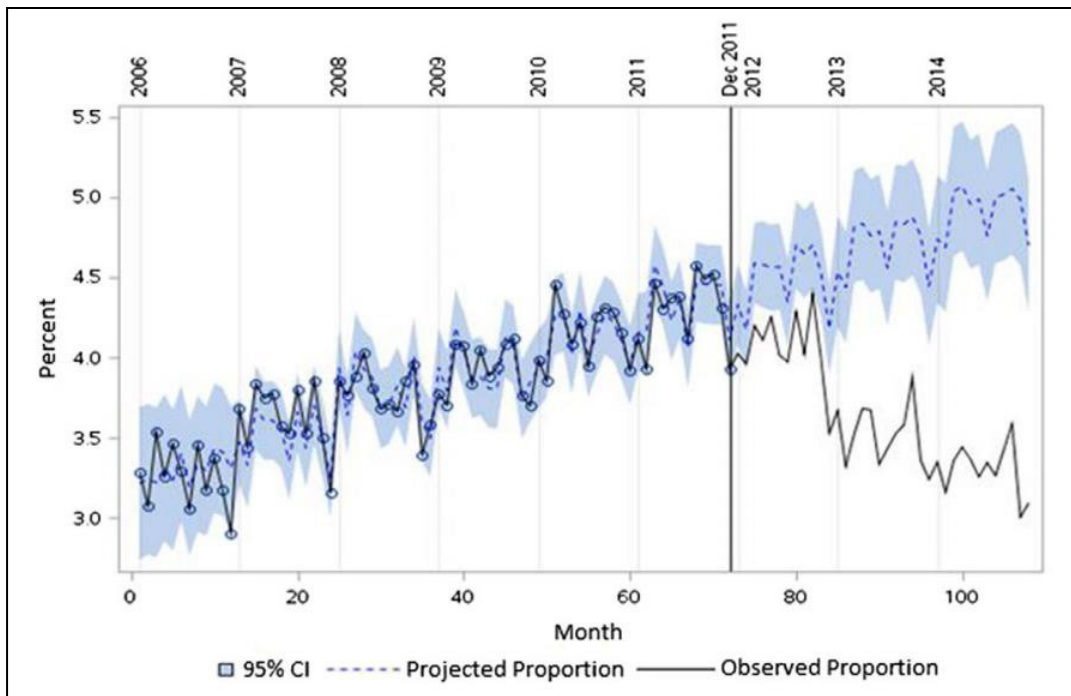
Figure 3. Monthly Forecasted Number versus Actual Proportion of Active Duty Members Receiving At Least One Opioid Prescription During 2006 To 2014

Table 3 presents the five interrupted time series models. Overall, troops returning from Operation Enduring Freedom (OEF), Operation Iraqi Freedom (OIF), or Operation New Dawn (OND) did not appear to influence the rates of use. Even after accounting for returning troops from OEF/OIF/OND and wounded in action counts, the deflection point was associated with a lower proportion of ADSMs who filled an opioid prescription, leading to a decrease of 1.61% by the end of the observation period (December 2014).

Table 3. Interrupted Time Series Analysis of Military System-Level Variables

	Model 1 Time Factors Only	Model 2 Wounded in Action Only	Model 3 OEF/OIF/OND Only	Model 4 Deflection Point Only	Model 5 All Variables
Intercept	3.552***	3.490***	3.565***	3.235***	3.132***
	(0.284)	(0.260)	(0.288)	(0.093)	(0.098)
Time	0.002	0.002	0.001	0.015***	0.016***
	(0.005)	(0.004)	(0.005)	(0.002)	(0.002)
Deflection point				−0.048***	−0.047***
				(0.007)	(0.005)
Δ OEF/OIF/OND (in thousands)			−0.003		0.004
			(0.002)		(0.002)
Wounded in action (in thousands)		0.261*			0.258*
		(0.121)			(0.114)
AR1	−0.384***	−0.382***	−0.379***	−0.242*	−0.225*
	(0.083)	(0.083)	(0.083)	(0.093)	(0.095)
AR3	−0.512***	−0.494***	−0.524***	−0.3925***	−0.393***
	(0.093)	(0.092)	(0.092)	(0.100)	(0.097)
AR4	0.101	0.100	0.104	0.151*	0.160*
	(0.063)	(0.064)	(0.064)	(0.069)	(0.067)
AR5	−0.136*	−0.157*	−0.132*	−0.105	−0.100
	(0.065)	(0.066)	(0.065)	(0.068)	(0.067)
AR12	−0.737***	−0.726***	−0.737***	−0.722***	−0.711***
	(0.058)	(0.058)	(0.058)	(0.065)	(0.064)
AR13	0.225*	0.240**	0.216*	0.145	0.158
	(0.087)	(0.087)	(0.087)	(0.098)	(0.099)
AR15	0.535***	0.523***	0.545***	0.430***	0.452***
	(0.091)	(0.090)	(0.090)	(0.096)	(0.094)
Goodness of fit					Best fit
Akaike Information Criteria	−105.5	−108.6	−106.3	−119.6	−126.0

Significance: ***0.001; **0.01; *0.05.

Sub-aim B

242,495 ADSM (43.8% Army, 83.9% male and 62.2% 18-25 years old) filled at least one opioid prescription during the study period. Individuals co-prescribed benzodiazepines or anti-depressants were significantly more likely to have LT LOW (benzodiazepine: 4.35 confidence interval (CI) [3.90, 4.86]; anti-depressant: 12.76 CI [11.32, 14.37]) and LT HIGH (benzodiazepine: 5.20 CI [4.44, 6.10]; anti-depressant: 23.05 CI [19.37, 27.43]) episodes. Patterns were similar for individuals with a major procedure, and those diagnosed with back pain, fractures, and musculoskeletal signs and symptoms. Compared to Army, ADSMs in the Air Force were significantly less likely to have any chronic use pattern (B-2). See table 4.

Table 4. Multinomial Logistic Regression Results by Type of Prescribing Episode

	Episodic aOR (95% CI)	Long-Term Low Dose aOR (95% CI)	Long-Term High Dose aOR (95% CI)
Systems Level factors			
Year (2012 vs 2013)	1.04 (1.02, 1.07)	1.10 (0.99, 1.22)	1.13 (0.97, 1.32)
Sponsor Service (Army as Reference)			
Navy	0.78 (0.75, 0.81)	0.54 (0.45, 0.64)	0.53 (0.40, 0.71)
Air Force	0.89 (0.85, 0.93)	0.91 (0.77, 1.07)	1.15 (0.92, 1.44)
Marines	0.88 (0.84, 0.91)	0.80 (0.69, 0.94)	0.90 (0.72, 1.14)
Sociodemographic Factors			
Sex			
M	0.88 (0.84, 0.91)	1.38 (1.20, 1.59)	4.67 (3.44, 6.34)
Age group (18-25 as reference)			
26-30	0.94 (0.90, 0.98)	1.11 (0.97, 1.28)	1.32 (1.08, 1.60)
31-34	0.96 (0.91, 1.02)	1.10 (0.92, 1.33)	1.43 (1.10, 1.85)
35 +	0.98 (0.94, 1.02)	1.01 (0.86, 1.18)	0.97 (0.76, 1.23)
Marital status			
Married	1.09 (1.06, 1.12)	1.13 (1.01, 1.26)	1.19 (1.00, 1.41)
Prescription History			
Benzodiazepine Prescription	2.12 (2.04, 2.21)	4.35 (3.89, 4.86)	5.20 (4.44, 6.10)
Antidepressant Prescription	2.51 (2.37, 2.66)	12.76 (11.32, 14.37)	23.05 (19.37, 27.43)
Healthcare Use			
Count of ER Visits	1.24 (1.22, 1.25)	1.35 (1.31, 1.39)	1.27 (1.22, 1.33)
Major Inpatient Procedure	1.63 (1.48, 1.80)	2.56 (1.99, 3.28)	7.67 (6.03, 9.75)
Unique Provider Count	1.06 (1.06, 1.07)	1.09 (1.07, 1.10)	1.12 (1.10, 1.14)
Psychosocial			
Substance use diagnosis (PSY02)	1.17 (1.08, 1.26)	1.41 (1.18, 1.68)	2.68 (2.19, 3.28)
Tobacco use diagnosis (PSY 03)	1.12 (1.07, 1.16)	1.53 (1.36, 1.72)	1.02 (0.85, 1.22)
Physical			
Musculoskeletal signs and symptoms (MUS 01)	1.37 (1.33, 1.41)	1.83 (1.63, 2.05)	2.11 (1.77, 2.52)
Acute Sprains and Strains (MUS 02)	1.24 (1.20, 1.28)	1.16 (1.03, 1.30)	0.90 (0.76, 1.07)
Fractures-excluding digits (MUS 04)	1.36 (1.29, 1.43)	1.87 (1.60, 2.18)	3.57 (2.94, 4.34)
Cervical pain syndromes (MUS 13)	1.05 (0.99, 1.11)	1.02 (0.87, 1.19)	0.94 (0.74, 1.18)
Headaches and Migraines (NUR 02 & NUR 22)	0.99 (0.94, 1.04)	0.87 (0.75, 1.01)	0.64 (0.52, 0.81)
Head injury (NUR 15)	1.10 (1.02, 1.18)	0.94 (0.76, 1.16)	1.07 (0.83, 1.38)
Burns--2nd and 3rd degree (REC 04)	1.15 (0.97, 1.36)	1.03 (0.59, 1.82)	1.80 (1.00, 3.23)
Low Back Pain (MUS14)	1.14 (1.10, 1.18)	1.88 (1.68, 2.10)	2.17 (1.84, 2.56)

ER = emergency room; aOR = adjusted odds ratio.

8.0   CONCLUSION/DISCUSSION

Sub-aim A
Here we utilized an innovative model (5x5x3) to determine the presence of aberrant drug taking behavior among ADSMs at rates comparable to those in the civilian sector. When the model is applied to PDTS data, the presence of aberrant drug taking behavior among ADSMs are at rates comparable to those in the civilian sector. In the context of military populations, alternative algorithms may be more appropriate.

We detected a significant reduction in opioid use patterns after December 2011 in both civilian and ADSM (nondeployed) populations, which was more pronounced in the military than civilian populations. Many factors, such as fewer wounded in action counts, may be reasons for these findings. Our results likely reflect a complex combination of many factors inside and outside of the military, including policy directives and cultural changes.

Sub-aim B
Sociodemographic and clinical variables associated with long-term opioid use were consistent with civilian and military populations. LT HIGH dose episodes resulted in a distinct pattern, suggesting efforts to reduce overall MME may be important in reducing risk. Potentially modifiable risk factors include concurrent prescribing of central nervous system (CNS) drugs during an opioid episode. Effects of concurrent benzodiazepine were less than other prescriptions; however, prevalence among ADSM suggests addressing concurrent benzodiazepine prescribing.

Overall, we were able to successful develop and test prescription database algorithms, utilizing a model developed and implemented successfully with civilian PMPs (5x5x3) despite our setbacks. We believe that this model and alternative thresholds warrants continued investigation using mixed-methods to identify an optimal risk threshold for PMP application within the MHS. However, due to the three technical challenges previously mentioned in section 5.2, we postponed on updating the analysis until we find a way to resolve the issue.

While we have identified empirical models using both pharmacy and medical claims data to predict opioid misuse and to assess early warning signs of opioid related problems, additional research is needed to examine the effects of multiple CNS drugs and opioid treatment for non-cancer pain.

In conclusion, when compared to the civilian sector, opioid use occurs less often in ADSMs. Continued development and refinement of MHS's and VA's PMPs will be required to achieve long-term solutions while reducing risks associated with opioid use and identify early warning signs of opioid related problems in military populations.

9.0   DELIVERABLES

9.1   Publications (A-1)

1) Kazanis, W., Pugh, M. J., Tami, C., Maddry, J. K., Bebarta, V. S., Finley, E. P., Potter, J. S., "Opioid Use Patterns Among Active Duty Service Members and Civilians: 2006–2014." *Military Medicine*, Vol 183, No. 3-4, e157-e164. 2018
2) Kazanis, W., Pugh, M. J., Tami, C., Maddry, J. K., Bebarta, V. S., Carnahan, D., Finley, E. P., McGeary, D., Potter, J. S., "Identify Modifiable Risk Factors to Facilitate Opioid Risk Mitigation," [*in preparation for submission*].

9.2   Presentations (B1-11)

1) 2 poster presentations at 2016 Military Health System Research Symposium (MHSRS)
2) Symposium at the 2016 SURF
3) Oral presentation at 2017 College on Problems of Drug and Dependence (CPDD),
4) 4 Poster presentations at 2017 MHSRS
5) 2 poster presentations at 2017 SURF
6) Poster presentation at 2017 Behavior, Biology, and Chemistry: Translational Research in Addiction (BBC)
7) Poster presentation at 2018 CPDD

10.0   COST

This work was funded by the Substance Abuse Working Group (SAWG) of the Joint Program Committee 5 (JPC-5) / Military Operational Medicine Research Program (MOMRP), US Army Medical Research and Materiel Command (USAMRMC). FY15 funding under Project Air Force Research Laboratory FA8650-15-C-6588-P1 of $617,635.00 was received January 2015 and all funds were expended by January 2018.

Appendix A

Appendix A-1: Opioid Use Patterns Among Active Duty Service Members and Civilians: 2006–2014

Appendix B

Appendix B-1: Predictors Of Long-Term Opioid Use In Active Duty Military: Psychotropics, Procedures, Pain

Appendix B-2: Chronic Pain and Substance Abuse: What's the Connection?

Appendix B-3: Predictors of Long-term Opioid Use in Active Duty Military: Psychotropics, Procedures, Pain

Appendix B-4: Applying civilian Prescription Drug Monitoring Program (PDMP) algorithms to prescription records from the Pharmacy Data Transaction Services (PDTS)

Appendix B-5: Factors and Policies Affecting Opioid Prescribing Patterns in Active Duty Patients between 2006 and 2014

Appendix B-6: Benzodiazepine use among low back pain patients concurrently prescribed opioids in the military health system

Appendix B-7: Time to Event Analysis of Long Term Opioid Use in the Active Duty Population

Appendix B-8: Benzodiazepine Use Among Low Back Pain Patients Concurrently Prescribed Opioids In The Military Health System Between 2012 Or 2013

Appendix 9: Predictors of Long-Term Opioid Use in Active Duty Military: Psychotropics, Procedures, Pain

Appendix B-10: Factors and Policies Affecting Opioid Prescribing Patterns in Active Duty Patients between 2006 and 2014

Apprendix B-11: Which factors are associated with first opioid and first benzodiazepine prescription in the military health system

B-1

Predictors Of Long-Term Opioid Use In Active Duty Military: Psychotropics, Procedures, Pain

William Kazanis, MS[1,2], Claudina Tami, BS[1], Mary Jo Pugh, PhD RN[1,2], Don McGeary, PhD[1], Erin P. Finley, PhD, MPH, Maj Joseph Maddry, MD[3,5,6], Vik Bebarta, MD[3,7], David Carnahan, MD[4,6], Jennifer Sharpe Potter, PhD MPH[1]

[1] The University of Texas Health Science Center at San Antonio, [2] South Texas Veterans Health Care System, [3] San Antonio Military Medical Center, [4] Defense Health Agency, [5] United States Air Force Medical Support Agency, [6] San Antonio Uniformed Services Health Education Consortium, [7] University of Colorado

Background: In the United States, chronic pain is more prevalent among active duty (AD) military service members (44%) than civilians (26%). Assessing factors associated with acute versus 3 long-term opioid use patterns (episodic, long-term low dose [LTLD], long-term high dose [LTHD]) may facilitate opioid risk mitigation. We predicted differences in system-level, clinical and opioid characteristics among opioid use patterns.

Materials and Methods: Administrative de-identified data (2012-2013) from the TRICARE Pharmacy Data Transaction Service and M2 DataMart included prescription information and diagnosis codes. Inclusion criteria: AD enrolled in TRICARE for $\geq$ 11 months who received ≥ 1 opioid in a year. Opioid episodes defined as: *Acute* (< 3 months) and episodes greater than 3 months: *episodic* (<120 days supply/10 prescriptions), *LTLD* (>120 days supply/10 prescriptions, average MME <20mg), *LTHD* (same as LTLD except average MME >20mg).

Results: Multinomial logistic regression identified risk factors associated with episodes (acute episodes as comparator). Cohort included 242,578 AD (43.8% Army, 83.9% male and 62.2% 18-25 years old). Individuals co-prescribed benzodiazepines were significantly more likely to have LTLD (4.36 CI[3.90, 4.86]) and LTHD (5.18 CI[4.45, 6.03]). Similarly individuals co-prescribed antidepressants were significantly more likely to have LTLD (13.63 CI[12.09, 15.37]) and LTHD (19.60 CI[16.60, 23.15]). Similar patterns were found for AD Army (vs. Air Force and Navy), and individuals who had major inpatient procedures or back pain.

Conclusions: Results are similar to that observed in civilians. Factors exist that are unique to military context, e.g., service branch. Areas of concern and potential modifiable risk factors include co-prescribing.

The views expressed are those of the author and do not reflect the official views or policy of the Department of Defense, Department of Veterans Affairs, or its Components.

B-2

Meeting: SURF, San Antonio, Texas. 2016

Chronic Pain and Substance Abuse: What is the Connection?

Moderator:
Jennifer Sharpe Potter, PhD, MPH, Associate Professor in the Departments of Psychiatry and Anesthesiology and Assistant Dean for Research and Student Programs in the School of Medicine at the University of Texas Health Science Center at San Antonio. Her primary research interest is substance use disorders. Her current research focuses on the prevention and treatment of opioid use disorders and chronic pain utilizing combined behavioral and medication-based approaches.

Moderator:
Sandra Valtier, PhD, Clinical Research Division 59th Medical Wing, Wilford Hall Medical Center, Lackland AFB, Dr. Valtier directs the Substance Abuse Task Area for the US Air Force and serves on the Army Substance Abuse Research Program advisory board. In this capacity show

Speaker 1:
Mary Jo Pugh, RN, PhD, Associate Professor of Epidemiology and Biostatistics, University of Texas Health Science Center at San Antonio and Veterans Evidence-based Research, Dissemination, and Implementation Center (VERDICT), South Texas Veterans Health Care System. Her research interests and background includes exploration of quality of care and health care system factors associated with patients with complex comorbidity clusters, especially older veterans and younger veterans from Afghanistan and Iraq Wars (OEF-OIF). She has used methods from pharmacoepidemiology and health services research to examine quality of care issues related to medication treatment approaches, comparative effectiveness, epilepsy care, and chronic disease management in older patients and my current work uses similar methods to understand OEF-OIF veterans and their healthcare needs.

Speaker 2:
Erin Finley, PhD, MPH, Assistant Professor of Medicine and Psychiatry, Division of Clinical Epidemiology. Dr. Finley is also an Investigator with the Veterans Evidence-based Research Dissemination and Implementation Center (VERDICT) at the South Texas Veterans Health Care System, and an Adjunct Assistant Professor with the Division of Clinical Epidemiology, Department of Medicine, at the University of Texas Health Science Center at San Antonio. Her primary research interests include PTSD and the implementation of evidence-based treatments for Veterans, interventions promoting resilience for individuals and families, and the role of social relationships in shaping health behaviors and outcomes.

Speaker 3:
Donald McGeary, PhD, ABPP, Associate Professor of Psychiatry, University of Texas Health Science Center San Antonio. Dr. McGeary is board certified in Clinical Health Psychology, American Board of Professional Psychology. His primary interests include interdisciplinary chronic pain intervention and military trauma. The majority of his experience and expertise has

been focused on chronic pain rehabilitation research and clinical work in multi- and interdisciplinary environments.

Objectives of the session:
Using results from an ongoing DoD and NIH studies as a backdrop, the objectives of the session are to:
- Describe the prevalence of co-occurring chronic pain and substance use disorder, specifically prescription-related opioid use disorder, among active duty service members
- Identify challenges and opportunities for implementing systems-level prevention and intervention initiatives in the Military Health System
- Explore treatment options for co-management of chronic pain and opioid misuse/abuse/addiction
- Provide a vehicle for discussion of research priorities in this area including a discussion of the Substance Abuse Task Area and current military research priorities in this area

The United States is experiencing a major public health crisis as a result of the dramatic rise in opioid prescriptions for chronic pain management during the last two decades. This includes a dramatic increase in opioid-related emergency department visits, poisoning deaths, opioid-related addiction treatment, and suicides.

The military is not immune increased opioid prescribing and potential adverse consequences. The 2009 Department of Defense (DoD) Survey of Health Related Behaviors among Active Duty Military Personnel revealed substantial increases in misuse of prescription drugs, attributed overwhelmingly to opioid analgesics. DoD rates were significantly higher than civilian rates of prescription drug misuse during the same period. In the Army, oxycodone and hydrocodone are the second and third most commonly prescribed analgesics.

Given the high prevalence of musculoskeletal pain, posttraumatic stress disorder, and depression in Iraq and Afghanistan military personnel post deployment, this cohort may be at increased risk for opioid misuse. In 2008, 10.1% of active duty military personnel reported misusing opioids in the prior month while 17.2% misused in the preceding 12 months. More recent survey data from a large MHS, supports these estimates. In an anonymous survey of patients presenting at an MHS emergency department (ED) and a Level 1 trauma center with an annual volume of 75,000 pts/year, 31% of active duty respondents reported opioid misuse (use of an opioid for reasons other than pain, use of an old opioid prescription for a new reason, or use of more medication than prescribed).

The session will be a combination of didactics, case study presentation, and facilitated group discussion. All didactics will draw from the peer-review literature and the presenters' own research data. During the session, we will be distributing index cards and using social media (e.g., live Tweeting) to solicit questions from the audience for use as discussion prompts. Each presentation will be followed by a Q&A session.

Presentations:

1. Jennifer S Potter, PhD: (co-moderator) Chronic pain and opioid use risk mitigation

Present summary of the current literature oh co-occurring chronic pain and opioid use disorder and an introduction to learning objectives
2. Sandra Valtier, PhD: (co-moderator) DoD Substance Abuse Task
   Discuss the current priorities of substance abuse task area research portfolio
3. Mary Jo Pugh, PhD: Opioid prescribing patterns in the US military: 2006-2014
   Report on patterns of opioid prescribing in the MHS using data from the DoD UT Health Science Center Opioid Risk Mitigation Project
4. Erin Finley, PhD: Systems level approaches to opioid risk mitigation in the MHS
   Present qualitative research findings on barriers and facilitators to implementing an opioid risk mitigation program in the MHS based on results from the DoD UT Health Science Center Opioid Risk Mitigation project
5. Donald McGeary, PhD: Behavioral pain management and reducing opioid misuse
   Describe nonpharmacological approaches to pain management that may reduce overall opioid misuse and, potentially, opioid misuse and abuse.

Abstract:
Using results from an ongoing DoD and NIH studies as a backdrop, the objectives of the session are to:
- Describe the prevalence of co-occurring chronic pain and substance use disorder, specifically prescription-related opioid use disorder, among active duty service members
- Identify challenges and opportunities for implementing systems-level prevention and intervention initiatives in the Military Health System
- Explore treatment options for co-management of chronic pain and opioid misuse/abuse/addiction
- Provide a vehicle for discussion of research priorities in this area including a discussion of the Substance Abuse Task Area and current military research priorities in this area

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The session will be a combination of didactics, case study presentation, and facilitated group discussion. All didactics will draw from the peer-review literature and the presenters' own research data. During the session, we will be distributing index cards and using social media (e.g., live Tweeting) to solicit questions from the audience for use as discussion prompts. Each presentation will be followed by a Q&A session.

B-3

Predictors of Long-term Opioid Use in Active Duty Military: Psychotropics, Procedures, Pain

JS. Potter, PhD MPH[1], MJ. Pugh, PhD RN[1,2], Maj J. Maddry, MD[3,5,6], D. Carnahan, MD[4,6] V. Bebarta, MD[3]

[1]The University of Texas Health Science Center at San Antonio, [2]South Texas Veterans Health Care System, [3]San Antonio Military Medical Center, [4]Defense Health Agency, [5]United States Air Force Medical Support Agency, [6]San Antonio Uniformed Services Health Education Consortium; University of Colorado

BACKGROUND: In the United States, chronic pain is more prevalent among active duty (AD) military service members (44%) than civilians (26%). Assessing factors associated with acute versus 3 long-term opioid use patterns (episodic, long-term low dose [LTLD], long-term high dose [LTHD]) may facilitate opioid risk mitigation. We predicted differences in system-level, clinical and opioid characteristics among opioid use patterns.

METHODS: Administrative de-identified data (2012-2013) from the TRICARE Pharmacy Data Transaction Service and M2 DataMart included prescription information and diagnosis codes. Inclusion criteria: AD enrolled in TRICARE for $\geq$ 11 months who received $\geq$1 opioid in a year. Opioid episodes defined as: *Acute* ($<$ 3 months) and episodes greater than 3 months: *episodic* ($<$120 days supply/10 prescriptions), *LTLD* ($>$120 days supply/10 prescriptions, average MME $<$20mg), *LTHD* (same as LTLD except average MME $>$20mg).

RESULTS: Multinomial logistic regression identified risk factors associated with episodes (acute episodes as comparator). Cohort included 242,578 AD (43.8% Army, 83.9% male and 62.2% 18-25 years old). Individuals co-prescribed benzodiazepines were significantly more likely to have LTLD (4.36 CI[3.90, 4.86]) and LTHD (5.18 CI[4.45, 6.03]). Similarly individuals co-prescribed antidepressants were significantly more likely to have LTLD (13.63 CI[12.09, 15.37]) and LTHD (19.60 CI[16.60, 23.15]). Similar patterns were found for AD Army (vs. Air Force and Navy), and individuals who had major inpatient procedures or back pain.

CONCLUSIONS: Results are similar to that observed in civilians. Factors exist that are unique to military context, e.g., service branch. Areas of concern and potential modifiable risk factors include co-prescribing.

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B-4

Applying civilian Prescription Drug Monitoring Program (PDMP) algorithms to prescription records from the Pharmacy Data Transaction Services (PDTS)

Authors: Jennifer Sharpe Potter Ph.D., M.P.H., William Kazanis M.S., Mary Jo Pugh Ph.D., Kristen Rosen Ph.D., Vikhyat S. Bebarta, MD, Joseph K. Maddry M.D.

Background: In support of opioid risk mitigation efforts, 49 states and Washington DC maintain Prescription Drug Monitoring Programs (PDMPs) that monitor opioid prescriptions and seek to identify anomalous patterns that may indicate misuse and abuse of prescription drugs. As such, PDMPs are potential valuable tools to 1) identify misuse and 2) trigger education and intervention initiatives. A critical issue is the algorithm use to identify misuse. A common threshold used by PDMPs is the "5x5x3", that is, 5 or more prescriptions from 5 or more prescribers in the course of 3 months. Currently, state run PDMPs do not capture opioids dispensed within the Military Health System (MHS). As part of a project exploring the feasibility of implementing a PDMP-like system with the MHS, we applied the 5x5x3 algorithm to Pharmacy Data Transaction Services (PDTS data) for active duty members of the US Armed Forces. It is possible that the civilian algorithm is not optimal to identify aberrant drug taking behavior among active duty military.

Methods: We used a de-identified PDTS dataset for all patients, prescribers and dispensers with prescription records (grouped monthly). All active duty service members receiving at least 1 opioid prescription between 2008 and 2014 were included. Using this data, we created a running count of providers and dispensers for the previous three months, every month, for 84 months between January 2008 and December 2014. This running count provided the number of providers and dispensers for the given month and the previous two months (three months total), each month, for any patient that received and opioid prescription in a given month. Once this was created, a count of unique patients crossing the 5x5x3 threshold each year was computed. Alternative existing algorithms, e.g., 10x10x3 and 5x5x6, and exploratory algorithms, based on input from MHS providers and leadership, were also implemented. This was to compare PDTS results and explore whether the 5x5x3 is the optimal algorithm for use in the MHS.

Results: Between 2008 and 2014, as many as 1,711 or 0.463% (i.e., in 2011) of active duty patients met or exceeded the 5x5x3 threshold within a year. After 2012, there appears to be a noticeable drop in individuals from the 2011 peak. By 2014, 666 (0.211%) active duty patients crossed the 5x5x3 threshold. For comparison purposes, in the Florida PDMP the count of those individuals prescribed a schedule II, III, or IV drug, 0.461% exceeded the 5x5x3 threshold.

Conclusion: The 5x5x3 algorithm, when applied to PDTS data, suggests the presence of aberrant drug taking behavior among active duty service members at rates comparable to those in the civilian sector. However, alternative algorithms may be more appropriate in the military context.

B-5

Factors and Policies Affecting Opioid Prescribing Patterns in Active Duty Patients between 2006 and 2014

William Kazanis M.S., Mary Jo Pugh Ph.D., Samantha Paniagua B.A., Vikhyat S. Bebarta, MD, Joseph K. Maddry M.D., Jennifer Sharpe Potter Ph.D., M.P.H.

Background: Prescription opioid misuse in the United States is currently a public health epidemic. This epidemic extends to our armed forces where prescription drug misuse, especially prescription opioid misuse, went up from 2% in 2002 to 4% in 2005. In June 2009 the office of the Surgeon General of the Army issued guidance to providers caring for patients receiving treatment for pain with multiple medications. This led to the creation of the pain management task force in August of 2009 and a comprehensive plan which was implemented in March of 2011. Due to concern for prescription opioid misuse and the military's efforts to curb misuse we examined opioid prescribing trends and patterns included in PDTS (Pharmacy Data Transaction Service) records for all active duty members that received at least 1 opioid prescription between January 2006 and December 2014 to observe factors associated with change in prescription patterns over time, including an overall effect of population and policy changes.

Methods: Interrupted time series models were created to examine the changes that occurred before and after implementation of the pain management task force recommendations across three outcomes: total active duty opioid patients per month, total opioid prescriptions per month given to active duty patients, and the proportion of active duty members of the armed forces that received an opioid prescription in a given month. Additional models investigated other factors that occurred over the same period including the active duty population, the OEF/OIF/OND boots on the ground population, wounded in action counts, and auto regressive, moving average and seasonal effects.

Results: From January 2006 through December 2014, 1,548,206 active duty patients received 7,073,743 opioid prescriptions. The results from the interrupted time series analysis showed significant drops in opioid prescriptions, patients, and percentages of patients in a given month after the new policies were implemented. After implementation of the policy, 564 ($X^2=22.752$,p=<.001) fewer patients, 765 ($X^2=22.355$,p=<.001) fewer prescriptions, and a decrease of approximately 0.04% (Z=2.2263,p=<.0259) active duty members using opioids per month than would have been predicted otherwise. Additional models that incorporated variables for OEF/OIF/OND "boots on the ground", active duty, and wounded in action found the policy shifts were a significant factor as well. After accounting for the other factors mentioned above, significant seasonal effects were still found with values being typically lower in December and higher in October.

Conclusions: The policy shift, even when included in models with other variables appears to be a significant factor in decreasing the number of active duty patients prescribed opioids, percent of active duty patients prescribed opioids, and the number of prescriptions given to active duty

patients. Additionally, there are significant seasonal effects with values being typically lower in December and higher in October

B-6

Benzodiazepine use among low back pain patients concurrently prescribed opioids in the military health system

Megan Curtis, MA[1], William Kazanis, MS[1,2], Claudina Tami, BS[1], Mary Jo Pugh, PhD RN[1,2], Don McGeary, PhD[1], Erin P. Finley, PhD, MPH[2], Maj Joseph Maddry, MD[3,5,6], Vik Bebarta, MD[3,7], David Carnahan, MD[4,6], Jennifer Sharpe Potter, PhD MPH[1]

[1] The University of Texas Health Science Center at San Antonio, [2] South Texas Veterans Health Care System, [3]San Antonio Military Medical Center, [4]Defense Health Agency, [5]United States Air Force Medical Support Agency, [6]San Antonio Uniformed Services Health Education Consortium, [7]University of Colorado

Background: Dramatic increases in the amount of opioids prescribed for chronic non-cancer pain, particularly low back pain, exist among those served by the military health care system. The combination of opioids and benzodiazepines poses numerous safety risks for the patient including respiratory suppression, oversedation, and overdose. In a large national sample of veterans, risk of fatal overdoses increased when opioids and benzodiazepines were concurrently prescribed. Despite the justified concerns regarding the abuse liability and the long-term safety and efficacy of opioids for chronic pain, they continue to be commonly prescribed with benzodiazepines. For example, one study report that 18-38% of patients with an opioid prescription received a benzodiazepine. These high-risk prescribing patterns have contributed to the fatal overdose epidemic. There is scant evidence regarding opioid and benzodiazepine prescribing practices among active duty service members with low back pain. It is important to understand factors associated with benzodiazepine use in this population to identify those most vulnerable to safety issues. To this end, we investigated factors associate with concurrent opioid and benzodiazepine prescribing among active duty service members with non-malignant low back pain who started their first opioid episode in 2012 or 2013.

Methods: Study population included active duty service members: (1) not deployed at the time of care, (2) diagnosed with non-malignant low back pain and (3) received their first documented opioid prescription in the military health system in 2012 or 2013. Analyses were conducted on a de-identified dataset created by the Data Discovery, Analytics, and Research (DDAR) team within the Enterprise Intelligence Section (EI) within the Defense Health Agency (DHA) that was derived from the Military Health System Mart (M2). The dataset was approved by the institutional and Department of Defense regulatory agencies. A logistic regression analysis was conducted to examine the use of benzodiazepine with the following variables: sociodemographics, opioid characteristics, psychiatric and physical factors.

Results: The cohort was 42,253 active duty service members receiving opioids with a low back pain diagnosis. Overall, the sample was predominantly male (78.54%), and half were between the ages of 18-25 years olds (50.04%). The most common service branch was Army (51.72%). Results from logistic regression analysis indicated individuals prescribed a benzodiazepine were significantly more likely to be prescribed at least one long acting opioid: 1.71 CI[1.46, 1.99]

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versus short-acting, receive chronic opioid therapy (>90 days): 2.39 CI[2.24, 2.56], and also have been prescribed an antidepressant: 2.07 CI[1.89, 2.28]. Additionally, those prescribed a benzodiazepine were significantly more likely to be diagnosed with a substance use disorder: 1.29 CI[1.13, 1.47].

Conclusion: Our findings suggest that differences in patient characteristics across a variety of domains may raise safety concerns and quality of care issues. The results are consistent with previous findings among both US veterans and civilian populations. To our knowledge, this is among the first to examine factors associated with benzodiazepine use in a low back pain population receiving opioids.

The views expressed are those of the author and do not reflect the official views or policy of the Department of Defense, Department of Veterans Affairs, or its Components.

Learning Objectives:
- Describe the safety concerns regarding benzodiazepine concurrently prescribed with opioids.
- Examine characteristics that differentiate between those who are or are not prescribed a benzodiazepine while receiving chronic opioid therapy.
- Demonstrate how analysis of administrative data sets sheds light on real world challenges.

Research Topic:
- Health Services Research Across DoD

B-7

Time to Event Analysis of Long Term Opioid Use in the Active Duty Population

William Kazanis, M.S.; Capt Mary Jo Pugh, USAF, Ph.D., NC (RET); Claudina Tami, B.S.; Maj Joseph K. Maddry, USAF, M.D., MC; Lt Col Vikhyat S. Bebarta, Colorado Air National Guard, M.D., MC; Erin P. Finley, Ph.D., M.P.H.; Don D. McGeary, Ph.D.; Col David H. Carnahan, USAF, M.D., MSCE; Jennifer Sharpe Potter, Ph.D., M.P.H.

Background: There is a high incidence of chronic pain in the military. More than 50,000 soldiers were wounded in action in Operation Enduring Freedom, Operation Iraqi Freedom, and Operation New Dawn. Additionally, 40% of soldiers report chronic pain after returning from deployment. Opioid therapy frequently plays a key role in pain management which may lead to prolonged opioid use spanning years after an injury. To understand factors affecting the duration of chronic opioid use, time to event analysis was used to determine factors increase or decrease the duration of chronic opioid episodes.

Methods: Data containing opioid prescription histories was used to define episodes of opioid use for active duty service members between 2006 and 2014. An episode in this analysis began when an individual received their first prescription and terminated when no further opioids were administered for at least six months afterward. A cohort was defined of all individuals who a) received opioids for at least 3 months b) received at least one opioid between January 2014 and May 2014 c) did not receive an opioid for six months following their last opioid prescription between January 2014 and May 2014 and d) did not have an opioid episode prior to this episode. Factors included in our model included a major procedure flag, count of Emergency room visits, number of unique providers, low back pain flag, a substance abuse flag, a co-occurring anti-depressant or benzodiazepine prescription flag, average milligram morphine equivalent (MME) greater than 50 flag, and a long acting opioid formulation flag. Cox proportional hazards models stratified by service branch were fit to determine factors that affect duration of opioid use.

Results: 4276 episodes were included in this analysis (Army 50%, Air Force 17%, Marines 12%, and Navy 21%). Each branch displayed separate effects. MME {Army (HR=.49;CI=[.39,.62]), Air Force (HR=.29;[.17,.49]), Marines (HR=.43; CI=[.32,.80]), Navy (HR=.46; CI=[.30,.72])} and antidepressant prescriptions {Army (HR=.52; CI=[.46,.62]), Air Force (HR=.56; CI=[.39,.81]), Marines (HR=.43; CI=[.29,.62]), Navy (HR=.47; CI=[.36,.61])} during an episode were significant across all branches. Emergency room visits were significant for the army (HR=.91; CI=[.88, .95]) and Marines (HR=.88; CI=[.81,.96]). Unique provider counts were significant for the army (HR=.97; CI=[.96, .99]) and Air Force (HR = .94; CI=[.91,.96]); and a substance abuse diagnosis was significant for the Army (HR = .73; CI=[.61, .86]) and Air Force (HR=.54; CI=[.31, .95]). The Army showed individuals over age 25 had longer episodes {26-30 (HR=.84; CI=[.75,.94]), 31-34 (HR=.83; CI=[.71,.97]), Over 35 (HR=.73; CI=[.64,.83])}. The Navy showed major procedures (HR=.58; CI=[.36,.94]) and low back pain (HR=.77; OR=[.64,.92]) extended an opioid episode. The Marines showed significant effects for long

acting opioids (HR=.71; CI=[.52,.97]). The Air Force showed effects for Benzo prescriptions (HR=.73; CI=[.58,.90]).

Conclusions: High MME and co-prescriptions of antidepressants were associated with longer episode duration in the US military. Additionally, factors unique to each service branch were found that impact the duration of an opioid episode.

B-8

Benzodiazepine Use Among Low Back Pain Patients Concurrently Prescribed Opioids In The Military Health System Between 2012 Or 2013

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Background: Dramatic increases in the amount of opioids prescribed for chronic non-cancer pain, particularly low back pain, exist among those served by the military health care system. The combination of opioids and benzodiazepines poses numerous safety risks for the patient including respiratory suppression, oversediation, and overdose. In a large national sample of veterans, risk of fatal overdoses increased when opioids and benzodiazepines were concurrently prescribed. Despite the justified concerns regarding the abuse liability and the long-term safety and efficacy of opioids for chronic pain, they continue to be commonly prescribed with benzodiazepines. For example, one study report that 18-38% of patients with an opioid prescription received a benzodiazepine. These high-risk prescribing patterns have contributed to the fatal overdose epidemic. There is scant evidence regarding opioid and benzodiazepine prescribing practices among active duty service members with low back pain. It is important to understand factors associated with benzodiazepine use in this population to identify those most vulnerable to safety issues. To this end, we investigated factors associate with concurrent opioid and benzodiazepine prescribing among active duty service members with non-malignant low back pain who started their first opioid episode in 2012 or 2013.

Materials and Methods: Study population included active duty service members: (1) not deployed at the time of care, (2) diagnosed with non-malignant low back pain and (3) received their first documented opioid prescription in the military health system in 2012 or 2013. Analyses were conducted on a de-identified dataset created by the Data Discovery, Analytics, and Research (DDAR) team within the Enterprise Intelligence Section (EI) within the Defense Health Agency (DHA) that was derived from the Military Health System Mart (M2). The dataset was approved by the institutional and Department of Defense regulatory agencies. A logistic regression analysis was conducted to examine the use of benzodiazepine with the following variables: sociodemographics, opioid characteristics, psychiatric and physical factors.

Results: The cohort was 42,253 active duty service members receiving opioids with a low back pain diagnosis. Overall, the sample was predominantly male (78.54%), and half were between the ages of 18-25 years olds (50.04%). The most common service branch was Army (51.72%).

Results from logistic regression analysis indicated individuals prescribed a benzodiazepine were significantly more likely to be prescribed at least one long acting opioid: 1.71 CI[1.46, 1.99] versus short-acting, receive chronic opioid therapy (>90 days): 2.39 CI[2.24, 2.56], and also have been prescribed an antidepressant: 2.07 CI[1.89, 2.28]. Additionally, those prescribed a benzodiazepine were significantly more likely to be diagnosed with a substance use disorder: 1.29 CI[1.13, 1.47].

Conclusion: Our findings suggest that differences in patient characteristics across a variety of domains may raise safety concerns and quality of care issues. The results are consistent with previous findings among both US veterans and civilian populations. To our knowledge, this is among the first to examine factors associated with benzodiazepine use in a low back pain population receiving opioids.

Keywords: opioids, benzodiazepine, and low back pain

B-9

Predictors Of Long-Term Opioid Use In Active Duty Military: Psychotropics, Procedures, Pain

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Background: In the United States, chronic pain is more prevalent among active duty (AD) military service members (44%) than civilians (26%). Assessing factors associated with acute versus 3 long-term opioid use patterns (episodic, long-term low dose [LTLD], long-term high dose [LTHD]) may facilitate opioid risk mitigation. We predicted differences in system-level, clinical and opioid characteristics among opioid use patterns.

Materials and Methods: Administrative de-identified data (2012-2013) from the TRICARE Pharmacy Data Transaction Service and M2 DataMart included prescription information and diagnosis codes. Inclusion criteria: AD enrolled in TRICARE for ≥ 11 months who received ≥ 1 opioid in a year. Opioid episodes defined as: *Acute* (< 3 months) and episodes greater than 3 months: *episodic* (<120 days supply/10 prescriptions), *LTLD* (>120 days supply/10 prescriptions, average MME <20mg), *LTHD* (same as LTLD except average MME >20mg).

Results: Multinomial logistic regression identified risk factors associated with episodes (acute episodes as comparator). Cohort included 242,578 AD (43.8% Army, 83.9% male and 62.2% 18-25 years old). Individuals co-prescribed benzodiazepines were significantly more likely to have LTLD (4.36 CI[3.90, 4.86]) and LTHD (5.18 CI[4.45, 6.03]). Similarly individuals co-prescribed antidepressants were significantly more likely to have LTLD (13.63 CI[12.09, 15.37]) and LTHD (19.60 CI[16.60, 23.15]). Similar patterns were found for AD Army (vs. Air Force and Navy), and individuals who had major inpatient procedures or back pain.

Conclusions: Results are similar to that observed in civilians. Factors exist that are unique to military context, e.g., service branch. Areas of concern and potential modifiable risk factors include co-prescribing.

B-10

Factors and Policies Affecting Opioid Prescribing Patterns in Active Duty Patients between 2006 and 2014

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Background: Between 2001 and 2009, opioid analgesic prescriptions in the Military Health System (MHS) quadrupled to 3.8 million. The sheer quantity of opioid analgesics available set the stage for issues related to misuse, abuse, and diversion. To address this issue, the DOD implemented at least 20 directives between 2006 and 2012 to improve opioid prescribing trends. To characterize opioid use in the active duty population during this period (2006-2014), we examined opioid prescribing trends for active duty service members (ADSM), compared the trends in the civilian population and explored the potential role of military-specific factors in changes in opioid use in the MHS.

Methods: Annual prescription counts were compared for the general and active duty populations. Interrupted time series models were created to examine changes in the proportion of ADSM receiving an opioid prescription before and after December 2011. Additional models incorporated other military factors over the same period including returning OEF/OIF/OND troops, wounded in action, and auto regressive effects.

Results: Between 2006 and 2014, 1,516,979 active duty personnel filled 7,119,945 opioid prescriptions. Although both military and civilian populations had fewer prescriptions after 2011, the military population a larger decrease of prescriptions dispensed each year than the civilian population. Models measuring changes after 2011 showed significant changes in the proportion of ADSM that received at least 1 prescription in a given month leading to a decrease of 1.77% of ADSM receiving an opioid prescription and significant increases of .0264% for every thousand wounded in action service members.

Conclusions: Trends after 2011 were found to be significant even when included in models with other variables and appears to be a significant factor in decreasing the proportion of ADSM receiving an opioid prescription.

The views expressed are those of the author and do not reflect the official views or policy of the Department of Defense, Department of Veterans Affairs, or its Components.

B-11

Meeting: 80th annual CPDD, San Diego, California

Which factors are associated with first opioid and first benzodiazepine prescription in the military health system?

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Background. The military health care system has seen a dramatic increase in opioid prescriptions. Despite concerns regarding abuse liability and efficacy, they continue to be prescribed concurrently with benzodiazepines, which presents additional safety risks. There is limited research on current opioid and benzodiazepine prescribing practices among active duty service members (ADSM) with low back pain (LBP). To this end, we investigated factors associated with concurrent opioid and benzodiazepine prescribing among ADSM with LBP, in order to identify those most vulnerable to safety issues. **Methods.** Population included ADSM: not deployed at time of care, diagnosed with LBP, filled first opioid prescription in 2013, and did not receive a benzodiazepine prescription before 2013. Patients with a cancer diagnosis were excluded. Analyses were conducted using a de-identified dataset derived from the Military Health System Mart(M2) database. A logistic regression analysis was conducted to examine the concurrent use of opioids and benzodiazepine by sociodemographics, opioid characteristics, psychiatric and health care factors. **Results.** Cohort included 18,568 ADSMs, of which 1,560 filled their first opioid and benzodiazepine prescription in the same calendar month. Overall, the cohort was predominantly male (78.15%), between the ages of 18-25 years olds (57.69%), and Army service members (51.06%). Logistic regression determined gender (female aOR=0.70, CI[0.61,0.81]), age (>35 years old aOR=2.14, CI[1.75,2.61]), and sponsor service (Navy aOR=1.25, CI[1.09,1.44]) were significant predictors in concurrent first fill of opioid and benzodiazepine prescriptions. **Conclusion.** The results are consistent with previous findings among US veterans and civilian populations. To our knowledge, this is one of the first investigations to examine factors associated with benzodiazepine use in ADSMs with LBP receiving opioids. Opioid characteristics are not associated with differences in benzodiazepine prescribing. Future research should continue to explore the role of psychiatric conditions and benzodiazepine co-prescribing. Similarly, the relationship between gender and benzodiazepine must be better understood.

LIST OF SYMBOLS, ABBREVIATIONS AND ACRONYMS

10x10x3	10 prescribers x 10 dispensers x 3 month
5x5x3	5 prescribers x 5 dispensers x 3 month
5x5x6	5 prescribers x 5 dispensers x 6 month
ADSM	Active Duty Service Member
ANOVA	Analysis of Variance
aOR	Adjusted Odds Ratio
BBC	Behavior, Biology, and Chemistry: Translational Research In Addiction
CI	Confidence Interval
CNS	Central Nervous System
CPDD	College on Problems of Drug and Dependence
DDAR	Data Discovery, Analytics, and Research
DHA	Defense Health Agency
DoD	Department of Defense
EI	Enterprise Intelligence Section
IRB	Institutional Review Board
JCP-5	Joint Program Committee 5
LT HIGH	Long-Term High Dose
LT LOW	Long-Term Low Dose
MDR	Military Health System Data Repository
MHS M2	Management Analysis and Reporting Tool
MHS	Military Health System
MHSRS	Military Health System Research Symposium
MME	Milligrams Morphine Equivalent
MOMRP	Military Operational Medicine Research Program
OEF	Operation Enduring Freedom
OIF	Operation Iraqi Freedom
OND	Operation New Dawn
PDMP FORSCE	Florida Prescription Drug Monitoring Program
PDTS	Pharmacy Data Transaction Services
PMPs	Prescription Monitoring Programs
SAMHS	San Antonio Military Health System
SAWG	Substance Abuse Working Group
STVHCS	South Texas Veterans Health Care System
SURF	San Antonio Military Health Systems and Universities Research Forum
US	United States
USAMRMC	US Army Medical Research and Materiel Command