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Predictors of Improvements in Pain Intensity in a National Cohort of Older Veterans with Chronic Pain

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Abstract

Little is known about the factors associated with pain-related outcomes in older adults. In this observational study, we sought to identify patient factors associated with improvements in pain intensity in a national cohort of older veterans with chronic pain. We included 12,924 veterans receiving treatment from the Veterans Health Administration with persistently elevated numeric rating scale scores in 2010 who had not been prescribed opioids in the prior 12 months. We examined 1) percentage decrease over 12 months in average pain intensity scores relative to average baseline pain intensity score; and 2) time to sustained improvement in average pain intensity scores, defined as a 30% reduction in 3-month scores compared to baseline. Average relative improvement in pain intensity scores from baseline ranged from 25% to 29%; almost two-thirds met criteria for sustained improvement during the 12-month follow-up period. In models, higher baseline pain intensity and older age were associated with greater likelihood of improvement in pain intensity, while VA service-connected disability, mental health, and certain pain-related diagnoses were associated with lower likelihood of improvement. Opioid prescription initiation during follow-up was associated with lower likelihood of sustained improvement. The findings call for further characterization of heterogeneity in pain outcomes in older adults as well as further analysis of the relationship between prescription opioids and treatment outcomes.

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Keywords

Chronic pain; Veterans; Numeric Rating Scale; Aged; Analgesics; opioid

Introduction

The prevalence of chronic pain is estimated to be 10% to 20% in the general population¹, and chronic pain is especially common among veterans^{2,3}. Key predictors of pain-related disability include baseline functional impairment, psychiatric comorbidities, poor general health, stress, coping patterns, and according to most reviews, older age^{4,5}.

Unfortunately, although older adults are known to be at high risk for pain⁶, we know little about the natural history of chronic pain in older age. More specifically, little is known about the factors that are associated with both positive and negative outcomes over time related to pain and its treatment in this age group⁷. Older adults are often excluded from clinical trials, and when they are included, results are often not analyzed or reported by age. Importantly, older adults also have the highest prevalence of long-term use of analgesics (including opioids)⁸. While some studies suggest positive associations among older age, short-term opioid use, and reductions in pain intensity⁹, a number of studies have linked prescription opioid use with worse pain outcomes and other adverse events^{10,11}.

Forty-four percent of veterans nationally are age 65 or greater, and 21% are age 75 or greater; these proportions are expected to increase over the next five years¹². Thus, the aging veteran population is at especially high risk for pain-related problems. Over the past decade, as one component of a national pain strategy, the Veterans Health Administration (VHA) has collected pain intensity score information during routine care; veterans are administered the single-item, 11-point Numeric Rating Scale (NRS) pain intensity measure during most outpatient VHA healthcare encounters. We recently demonstrated that VHA pain intensity scores can be reliably extracted from the medical record and described over time. The primary objective of the current study was to identify patient demographic and clinical factors associated with change in NRS scores over time in a national cohort of veterans 65 years or older who have indicators of chronic pain (i.e., elevated pain intensity scores and pain-related diagnoses). A secondary objective was to identify factors associated with sustained improvement in NRS scores. Based on the prior literature available, we hypothesized that older age and comorbid mental health conditions would be associated with less improvement in pain over time.

Methods

The Institutional Review Board of the Portland VA Health Care System approved this study. The study was considered exempt from requiring written informed consent as it was a secondary analysis of existing data contained in VHA administrative datasets. Methods related to this project have previously been described.

Sources of Data

Pain intensity scores are recorded as structured vital sign data in VHA's electronic health record. Through VHA's national Corporate Data Warehouse (CDW), these data can be linked with outpatient and inpatient utilization, pharmacy, diagnosis, and demographic data. The CDW combines electronic health record data for all VHA patients from 1999 to present into a relational database. The VHA Informatics and Computing Infrastructure (VINCI) facilitates secure access to CDW data for approved VHA researchers.

Sample

To identify a national cohort of older (age 65) veterans with indicators of chronic pain, we began by obtaining a retrospective sample from the population of 5.9 million VHA patients with at least one VHA outpatient visit in 2010 (Figure). To be included in the study, patients had to have at least three average monthly pain intensity scores of 4 or greater (called "qualifying scores") within a 12-month period beginning in 2010. Each patient's NRS scores were averaged using all scores within each month to produce average *monthly pain intensity scores*. Computing monthly averages reduces the influence of months in which numerous pain intensity scores are reported that may not be reflective of a patient's usual pain experience. For study inclusion, qualifying scores could occur in any three months within the 12-month period. This operational definition of chronic pain is consistent with commonly used definitions for chronic pain of moderate or greater intensity of at least 90 days duration, as well as our, and other investigators' prior work. Each patient with three qualifying scores was assigned an index date, defined as the last day of the month in which the third qualifying score was obtained.

To focus on non-cancer pain, we excluded patients with documented International Classification of Diseases, Clinical Modification 9th edition (ICD-9-CM) cancer diagnoses in the 12 months prior to or following the index date (ICD-9-CM codes 140–208 and 230–239, which include malignant neoplasms and carcinomas *in situ*). We also excluded patients who had participated in VHA opioid substitution programs in the 12 months prior to or following the index date, patients who died during the 12 months after the index date, non-Veterans, and test patients.

We further refined the sample by selecting patients who had at least one ICD-9-CM pain diagnosis (Table 1) made by VHA clinicians during the 12 months prior to the index date. This refinement was guided by Tian et al.'s recently validated algorithm to identify chronic pain, which combines pain intensity scores and ICD-9-CM diagnostic codes; the addition of pain diagnoses to pain intensity score data improved accuracy in their analysis. In order to identify potential associations between opioid initiations and pain intensity scores over time, we excluded patients from our main cohort who had VHA opioid prescriptions dispensed during the 12 months prior to the index date. Finally, we excluded inactive VHA patients, defined as patients who did not receive any VHA prescriptions during the study year, as well as patients who did not have pain intensity scores in each of three different months (not necessarily consecutive) in the 12 months following their index dates, and patients (n=16) who had missing demographic data. After applying exclusion criteria, the final cohort included N=12,924 patients.

Measures

Dependent variables—Although there are known limitations due to variability in how the NRS is administered¹, the NRS remains a commonly-used standard as a brief measure of pain intensity, and has been validated in a number of patient populations². Our previous work showed that patients often have clinically meaningful variation in NRS scores within a given month; use of multiple scores over time may improve accuracy. Therefore, for our current primary analysis, the main dependent variable was percentage decrease in averages of three consecutive monthly pain intensity scores over time relative to the average baseline pain intensity score; thus, at least three monthly scores were required following the index date to compute the primary outcome. The baseline pain intensity score was defined as the mean of *all* average monthly pain intensity scores, beginning with the first qualifying score and ending with the index date.

For our secondary analysis, we measured time to sustained improvement in NRS monthly pain intensity score over 12 months of follow-up. A 30% reduction in NRS has been recommended as an indicator of meaningful clinical improvement in pain intensity. The month of sustained improvement was defined as the third month in the first set of three monthly pain intensity scores whose average was at least 30% lower than the baseline average NRS score.

Independent variables—Patient *demographic variables* included age (at index date), sex, race/ethnicity, marital status, VA service-connected disability status, and VHA facility. We selected values for these variables (other than age) using data available as of the date of the visit most immediately prior to the index date. At least one self-identified race designation was available for 90% of the cohort. Because Asian, Pacific Islander, Native American, and other races represented cumulatively only 3% of the sample, we collapsed these races into an “other” category. Ethnicity data included “not Hispanic or Latino,” “Hispanic or Latino,” “unknown,” and “declined.” We created five combined race/ethnicity categories: white (non-Hispanic), black (non-Hispanic), Hispanic/Latino, other (including multiple races), and unknown (including missing or declined).

Other Clinical variables—We also obtained pain and mental health diagnoses (including substance use disorder diagnoses and tobacco use) using ICD-9-CM codes documented in the 12 months prior to the index date (Table 1). We included the Selim comorbidity index³, which is a validated method for measuring medical comorbidity using ICD-9-CM diagnoses, in the 12 months prior to the index date. We also created a dichotomous variable to indicate whether a patient received major surgery in the 12 months prior to the index date, based on definitions from the American College of Surgeons National Surgical Quality Improvement Program (NSQIP). For the secondary analysis (see below), we also created a time-dependent variable for opioid prescription status indicating whether any opioid had been prescribed (yes/no) prior to each month in the analysis.

Analysis

To focus on chronic (as opposed to acute) pain, our analyses did not include NRS scores recorded during visits for surgical and medical procedures (VHA outpatient clinic codes

available on request) or scores that had been obtained during inpatient, residential, or nursing home stays. We also did not use scores obtained on days when multiple scores had been recorded. For example, multiple NRS scores from emergency department visits (as seen in 18% of patients in this cohort) could be associated with acute injury or illness; these scores may not be representative of chronic pain. Multiple scores from single days also had potential to overweight monthly average pain intensity scores.

To examine relationships between baseline patient characteristics and changes over time in average pain intensity scores, we first used longitudinal mixed models that allowed for correlations between patient scores. Here, we examined averaged effects of associations between baseline patient characteristics and changes in three-month average pain intensity scores over time, in which patient and facility were incorporated as random effects. These random effects allow for correlation between observations over time on the same patient and for correlation between patients treated at the same facility. We incorporated demographic variables (age, sex, race/ethnicity, marital status, VA service-connected disability status) and baseline clinical variables (baseline pain intensity score, Selim comorbidity score, and yes/no indicators of major surgery and pain and mental health diagnoses described above). The Selim score variable was collapsed into six categories (0–3, 4, 5, 6, 7, and 8) based on its frequency distribution, reducing the impact of a relatively few individuals with high (or low) Selim scores. Prescription opioid status was not used as a time-varying covariate because its inclusion would violate longitudinal assumptions (i.e., pain intensity scores would likely influence future opioid prescriptions). Due to potential concerns about accuracy of the NRS when cognitive problems are present, in a sensitivity analysis, we excluded veterans with documented diagnoses of dementia and other cognitive disorders (ICD-9-CM: 290.4–290.43; 293.0; 294.0; 294.1–294.11; 294.8; 294.9; 780.09).

We next examined hazard ratios for sustained improvement in monthly pain intensity scores, analyzed using Cox proportional hazards regression models (extended to allow for time-varying covariates) with censoring at last monthly pain intensity score during the one year follow-up period. The hazard ratios obtained provide estimated risk ratios for sustained improvement at any given month among individuals who have data at that month and have not previously obtained sustained improvement. So, when comparing two groups, hazard ratios greater than 1 indicate that the comparator group (in the numerator) has a greater chance of obtaining sustained improvement than the reference group (individuals who have not yet obtained sustained improvement). The month of sustained improvement was defined as the third month in the first set of three monthly pain intensity scores whose average was at least 30% lower than the baseline average NRS score. We incorporated prior opioid prescription status (yes/no: any active prescription for an opioid medication during the follow-up period, up to the month prior to the last month of the 3-month endpoint) as a time-varying covariate, as well as demographic and baseline clinical variables. We also incorporated the patient's VHA facility as a random effect via a (Gamma) shared-frailty model in order to allow for correlation between patients treated at the same location. Unadjusted hazard ratios and adjusted hazard ratios are provided. To assess the proportional hazards assumptions, graphical methods along with global tests using Schoenfeld residuals were used. In a sensitivity analysis, we used a 50%, rather than 30%, reduction in average 3-month pain intensity scores from baseline as the criterion for sustained improvement.

Results

After applying exclusion criteria, the final cohort included N=12,924 patients (Figure). Subjects on average were 73.1 (sd=7.2) years old and the majority were male (96%) (Table 2). The majority (64%) were identified as white, non-Hispanic and more than half (57%) were married. Sixty percent of patients had one or more service-related disabilities. Diagnosed non-substance-related mental health disorders including depressive disorders, anxiety disorders, or psychotic-spectrum disorders were common (41%). A majority of patients had been diagnosed with rheumatism, arthritis, or gout (65%) and chronic neck or joint pain (61%). Having multiple pain diagnoses in the year prior to the index date was the norm rather than the exception; the mean and median number of pain diagnoses were 2.5 and 2, respectively. The mean baseline pain intensity score was 5.6 (sd=1.6). Table 3 lists the numbers of subjects who had at least one pain intensity score in each of the 12 follow-up months, the number who had at least one pain intensity score in each of three prior months, and the number during each follow-up month who met criteria for sustained improvement at that month.

Changes in average pain intensity scores over time—longitudinal analysis

Table 4 provides model statistics for univariable and multivariable analyses examining associations between baseline patient characteristics and percentage change in average pain intensity scores following the index date, relative to average baseline pain intensity scores. The average relative improvement from baseline (using three-month averages) ranged from 25% to 29% over the follow-up months. Reductions in pain intensity were greater among the oldest subgroup of patients, widowed as compared to married patients, and for those with higher average baseline pain intensity scores. Pain intensity over follow-up worsened among patients having a VA service-connected disability, and those with diagnoses of substance use or other mental health disorders, and specific chronic pain diagnoses including low back pain, neuropathy, and fibromyalgia/myofascial pain.

Results remained relatively consistent across the multivariable analysis, which included all covariates evaluated in univariable analyses, as well as linear and quadratic effects of time (data not reported for time effects), but there were several exceptions. In the multivariable analysis, mental health diagnosis other than substance use disorder, and diagnoses of rheumatism/arthritis/gout, fibromyalgia/myofascial pain, lower back pain, and neuropathy were each associated with less improvement in pain over follow-up, while marital status and substance use disorder diagnosis were no longer associated with longitudinal changes in pain intensity. In the multivariate model, overall, higher Selim score tended to be associated with greater reductions in pain.

Time to sustained improvement—Cox proportional hazards analysis

We examined hazard ratios for sustained improvement in pain intensity. Included in these models was a variable representing prescription opioid use (yes/no) prior to the endpoint. Table 5 presents model statistics for associations of demographic and clinical characteristics with sustained improvement in pain intensity. Overall, a total of 8,335 patients (64.5% of the analytic sample) met criteria for sustained improvement at some point during the 12-month

follow-up. In univariate analyses, likelihood of sustained improvement was significantly greater among patients with higher average baseline pain intensity scores, widowed versus married patients, and patients in the older age categories. Higher Selim comorbidity scores, 50% or greater VA service-connected disability versus no service-connected disability, and diagnoses of substance use disorder or other mental health disorder, fibromyalgia/myofascial pain, lower back pain, neuropathy, and other musculoskeletal pain (excluding neck, joint, and low back pain) were each associated with decreased likelihood of sustained pain improvement. Initiation of prescription opioid therapy during the follow-up period was also associated with decreased likelihood of sustained improvement. In the multivariable model, the strength of associations of demographic and clinical characteristics with likelihood of sustained improvement in pain intensity remained commensurate or were only slightly attenuated. However, older age categories became only marginally significantly associated with sustained improvement, and marital status and Selim score were no longer statistically significant.

Additional Analyses

We conducted two planned sensitivity analyses: In the first analysis, in the Cox proportional hazards model, we used a 50%, rather than 30% reduction from baseline pain intensity score, as the criterion for sustained improvement. Here, there were no major changes in directionality or significance of the results (results not shown). In the second sensitivity analysis, in which we excluded subjects with documented dementia or other cognitive disorder diagnoses ($n=1,466$ or 11% excluded), there were also no substantive changes in directionality or significance of results (results not shown). In follow-up to our finding in the Cox models that opioids were associated with lower likelihood of improvement, we also conducted a *post hoc* analysis of the subgroup of veterans who were prescribed opioids during the study period ($n=3,149$); here we found that cumulative opioid dose greater than the median (vs. below the median) was associated with lower likelihood of improvement ($HR=0.79$, $p<0.0001$).

Discussion

This study is the first we have identified to examine correlates of changes over time in pain intensity scores obtained during routine practice from a national sample of patients with indicators of chronic pain. We used two modeling approaches, and the models produced similar results: baseline pain intensity and older age categories were associated with greater likelihood of improvement in pain intensity over time, while VA service-connected disability status, and mental health, chronic low back pain, neuropathy, and fibromyalgia/myofascial pain diagnoses were associated with lower likelihood of improvement. In the Cox models, we found that opioid prescription initiations were also associated with lower likelihood of improvement.

There is limited information on the natural history of pain in older persons. Overall, studies have shown mixed findings regarding the prevalence and course of pain when comparing age strata^{1,2,3,4}, but most reviews suggest that older age is a risk factor for worse pain outcomes. Findings from the current study indicate that, in contrast to these prior studies and our

hypothesis, older age within a cohort of individuals 65 and older who have chronic pain is associated with greater improvement in pain intensity over time. Almost two-thirds of this sample experienced a clinically significant improvement in pain intensity score sometime over the course of a year. There are a number of potential explanations for this. First, we looked *within* an overall group over age 65 which may have provided more age strata-specific data than prior studies. It is possible that individuals who are less healthy, and who perhaps have more pain, may not survive to enter the oldest age groups. Furthermore, prior research suggests that as age increases, the prevalence and perceptions of pain specific to various regions of the body may change, and that pain *interference* may increase. Adjustment to chronic pain has also been shown to vary by pain duration. Our study did not examine these outcomes or mechanisms; these issues are worthy of additional exploration.

We found that higher levels of baseline average pain intensity were associated with greater reductions in pain and with greater likelihood of sustained improvement. This finding may be due to the phenomenon of regression to the mean, as our cohort was selected based on specific indicators of chronic pain including average within-month pain intensity scores of 4 or greater over three separate months. It is possible that these score elevations may not have been representative of the entirety of patients' pain intensity experiences. Nonetheless, it could also be the case that pain treatments are more effective at helping patients move from high to moderate pain than from moderate to low pain, or that higher baseline pain intensity scores are associated with more acute problems or injuries which are more apt to resolve by themselves or with treatment as compared to sources of chronic pain.

We found that mental health conditions were frequently comorbid in our sample, and as we hypothesized, overall mental health conditions were risk factors for less improvement in pain over time and lower likelihood of sustained improvement. These results are consistent with prior work showing that patients with substance use disorders and other mental health conditions often experience greater pain intensity and functional interference relative to patients without these conditions, and are likely to have worse pain outcomes^{7, 8}. We also found that VA service-connected disability status was associated with less improvement in pain and greater time to sustained improvement. Several studies have shown relationships between disability compensation status and worse pain outcomes⁹. In our case, limitations of the data include that we were not able to differentiate between the various conditions for which patients had service-connected disabilities. Furthermore, there may have been additional, but unmeasured, factors that influenced disability compensation status.

We found that several pain diagnoses were consistently associated with less pain improvement and longer time to sustained improvement. These diagnoses included low back pain, neuropathy, and fibromyalgia/myofascial pain. It is possible that these pain syndromes are more likely to persist, or are less responsive to pain treatment compared to other diagnoses. They may also be more likely to be comorbid with one another; prior reviews suggest that multiple pain conditions are associated with worse pain outcomes. We note that we did not measure utilization of various types of pain treatment (non-opioid pharmacotherapy or non-pharmacologic therapies) in this study and were unable to determine if patients with poorer longitudinal pain outcomes were less likely to receive certain pain treatments, or received them but were less responsive.

Importantly, we found that in this patient population, on average, prescription opioid initiation was associated with lower likelihood of sustained improvement in pain intensity. This finding is consistent with several prior observational studies suggesting that the use of prescription opioids is associated with worse functional outcomes¹¹. In our study, the association between prior opioid therapy and likelihood of sustained improvement (in the Cox models) remained even after controlling for baseline pain intensity *within individuals*. Nonetheless, we cannot draw conclusions about causality given the observational nature of the study. In particular, we did not adjust for measured or unmeasured factors that might contribute to clinicians' decisions to prescribe opioids. Finally, it was beyond the scope of the current analysis to conduct a detailed exploration of the relationships of NRS scores with opioid dose, type of opioid (e.g. long-acting vs. short-acting) or duration.

There are additional limitations to this project worth noting. Importantly, results may have limited generalizability to non-VHA patient populations of older adults, younger patient populations, women, or patients *currently* prescribed opioid medications; it would be helpful to expand these analyses to other patient populations. Additionally, while the NRS remains a standard for briefly measuring pain intensity and has been validated in a number of clinical contexts and patient populations¹², little is known about how the NRS performs in clinical settings when administered by clinical personnel. Indeed, several investigations of VHA patient populations¹³ have shown that the accuracy of the NRS in measuring pain as administered during routine care is modest, and our and others' work suggests that single scores may have limited informational value¹⁴. For these reasons, we chose to measure multiple NRS scores over time such that any particular score would not be weighted too heavily in the analyses. We also did not exclude patients with dementia or other cognitive disorders in our primary analyses, which could impact reliability of the NRS; however, in our sensitivity analysis, we excluded subjects with prior diagnoses of these conditions, and did not see substantive impacts on results. We also chose to exclude patients with cancer diagnoses in the year prior to and during the study year. In our older patient population, this comprised approximately 15% of the potential sample, possibly further limiting generalizability. However, we note that patients with cancer are likely to have differing types of pain, pain treatments, and courses of pain compared to other patients with chronic pain.

Further, although we used methods similar to those of prior studies, there is no gold standard for identifying chronic pain using large administrative datasets. Measures of function are highly recommended for monitoring outcomes over time and for guiding treatment of chronic pain¹⁵. Unfortunately, functional measures are not currently available in national VHA datasets. While nearly two-thirds of the sample experienced a clinically significant improvement in pain intensity score over 12 months, we are unsure how stable these changes are, though our methodology for defining improvement required that improvement be sustained at least three months. Finally, we note that the cohort was selected based on data from 2010 and followed into 2011. During this time, advances in a stepped model of care and integrated behavioral approaches to pain management were being championed in VHA¹⁶, which could contribute to a cohort effect. However, this possibility would not explain the differences we found when comparing subgroups within the cohort.

National VHA pain intensity score data present a unique opportunity to learn more about the natural history of pain intensity, correlates of pain, and chronic pain outcomes in a large sample of individuals. We used two analytic approaches to working with these longitudinal data that yielded similar results. Higher baseline pain intensity and older age were associated with greater likelihood of reductions in pain intensity over time, while VA service-connected disability status, mental health, and certain pain-related diagnoses were associated with lower likelihood of pain intensity reductions. We also found that opioid prescription initiation during the follow-up period was associated with lower likelihood of improvement, though we were unable to adjust for opioid treatment selection bias. Notably, although nearly two-thirds of this sample experienced clinically meaningful reductions in pain intensity over 12 months, a substantial minority of veterans did not experience reductions in pain intensity and, in some cases, some experienced pain exacerbations. Indeed, some recent studies have shown that groups of patients with differing pain outcome trajectories can be identified and characterized¹⁸. Study findings call for further development of strategies that identify and target older individuals who have, or are more likely to have, treatment-refractory chronic pain. Additional research is needed to identify factors associated with changes in pain intensity in alternative patient populations, better understand mechanisms underlying heterogeneity in pain outcomes, and further examine the relationship between prescription opioids and treatment outcomes in older adults.

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Perspective

This study identified factors associated with improvements in pain intensity in a national cohort of older veterans with chronic pain. We found that older veterans frequently demonstrate improvements in pain intensity over time, and that opioid prescriptions, mental health and certain pain diagnoses are associated with lower likelihood of improvement.

HIGHLIGHTS

- Most older veterans with elevated pain intensity scores improved over time.
- Higher baseline scores and age were associated with greater likelihood of improvement.
- Mental health diagnoses were associated with lower likelihood of improvement.
- Opioid prescription initiation was associated with lower likelihood of improvement.
- Further study of heterogeneity in pain outcomes in older adults is needed.

Figure.
Development of the Study Cohort

Table 1

International Classification of Diseases, ninth edition, clinical modification (ICD-9-CM) codes used to identify pain-related and psychiatric diagnoses

Pain	
Rheumatism/Arthritis/Gout	274 – 274.99; 712 – 712.99; 714 – 716.99; 720 – 720.99; 729 – 729.09; 729.20 – 729.99
Chronic Neck/Joint Pain	716 – 719.99; 723 – 723.99; 729 – 729.09; 729.2 – 729.99
Chronic Lower Back Pain	722 – 722.99; 724 – 724.99
Other Musculoskeletal Pain	710 – 711.99; 713 – 713.99; 721 – 721.99; 725 – 728.99; 730 – 739.99
Neuropathy ^a	250.6 – 250.69; 337.0 – 337.19; 354 – 354.99; 356 – 357.99; 377 – 377.99
Headache or Migraine	346.9 – 346.99; 784.0
Fibromyalgia/Myofascial Pain	729.1
Psychiatric	
Major Depressive Disorder	296.20 – 296.39; 311 – 311.99
Schizophrenia or Bipolar Disorder	295 – 295.99; 296 – 296.09; 296.40 – 296.80; 296.89
PTSD	309.81
Anxiety or Panic Disorder	293.84; 300.00; 300.01; 300.02; 300.21; 300.22; 300.23; 300.29; 300.3; 308.3
Substance Use Disorder ^b	303.90 – 304.09; 304.20 – 304.49; 304.80 – 305.09; 305.20 – 305.29; 305.50 – 305.79; 305.90 – 305.99
Tobacco Use Disorder	305.1; 649 – 649.04

^aIncludes diabetic neuropathy and carpal tunnel syndrome

^bIncludes alcohol use disorders

Table 2

Demographic and clinical characteristics of study sample, N=12,924

Demographic and Clinical Characteristics	n (%) or M (SD)
Age	
65–69	5,549 (43%)
70–74	2,431 (19%)
75–79	2,258 (17%)
80–84	1,445 (11%)
85 or older	1,241 (10%)
Gender	
Male	12,463 (96%)
Female	461 (4%)
Race	
White, Non-Hispanic	8,213 (64%)
Black, Non-Hispanic	2,261 (17%)
Hispanic/Latino	756 (6%)
Other	578 (4%)
Unknown	1,116 (9%)
Marital Status	
Married	7,377 (57%)
Divorced/Separated	3,143 (24%)
Widowed	1,715 (13%)
Single/Never married	689 (5%)
Percent VA Service Connection	
None	5,127 (40%)
Less than 50%	1,804 (14%)
50% or more	5,993 (46%)
Selim Score	
0–3	1,997 (15%)
4	2,131 (16%)
5	2,511 (19%)
6	2,272 (18%)
7	1,651 (13%)
8	2,362 (18%)
Major Surgery	336 (3%)
Baseline Pain Intensity Score	
0–4	2,389 (18%)
5–6	5,917 (46%)
7–8	3,794 (29%)
8–10	824 (6%)
Tobacco Use Disorder diagnosis	1,513 (12%)
Substance Use Disorder diagnosis	925 (7%)

Demographic and Clinical Characteristics	n (%) or M (SD)
Other Mental Health Disorder diagnosis ^a	5,258 (41%)
Pain Diagnoses:	
Rheumatism/Arthritis/Gout	8,435 (65%)
Chronic Neck/Joint Pain	7,871 (61%)
Chronic Lower Back Pain	5,996 (46%)
Other Musculoskeletal Pain	5,614 (43%)
Neuropathy	3,184 (25%)
Headache or Migraine	978 (8%)
Fibromyalgia/Myofascial Pain	504 (4%)

^a Any mental health disorder excluding tobacco and substance use disorders.

Table 3

NRS pain intensity scores available during the follow-up period (n=12,924)

Follow-up Month	Had one or more NRS scores in this month	Had at least one NRS score in each of three different months, up to and including current month ^a	Number meeting criteria for sustained improvement ^b in each month ^a
1	5,885	----	----
2	5,825	----	----
3	6,134	1,679	776
4	6,041	2,339	952
5	5,836	2,687	948
6	6,211	2,988	1,049
7	5,934	2,982	970
8	5,737	2,849	850
9	5,731	2,834	825
10	5,704	2,636	734
11	5,751	2,531	640
12	5,630	2,432	591

^a Individuals meeting criteria for sustained improvement are removed from counts in future months.

^b The month of sustained improvement was defined as the third month in the first set of three monthly pain intensity scores, the average of which was at least 30% lower than the baseline average NRS score. The event rate was 8,335 events in the 25,957 months of follow-up = 0.32 events per month.

Table 4
Longitudinal Analysis: Reductions in average pain intensity scores over time relative to baseline, N=12,924

Variable	Univariable Analysis				Multivariable Analysis			
	Coefficient ^a	95% CI	p-value		Coefficient ^a	95% CI	p-value	
Age			<0.0001				<0.0001	
65 to 69 years (reference)								
70 to 74	3.22%	1.30, 5.14%	0.0010		1.11%	-0.80, 3.01%	0.2542	
75 to 79	4.66%	2.68, 6.63%	<0.0001		2.42%	0.43, 4.42%	0.0170	
80 to <85	6.43%	4.10, 8.77%	<0.0001		3.67%	1.30, 6.03%	0.0023	
85 or older	8.22%	5.74, 10.70%	<0.0001		6.45%	3.90, 9.00%	<0.0001	
Male sex	2.25%	-1.48, 5.98%	0.2369		3.53%	-0.17, 7.23%	0.0614	
Race/Ethnicity			0.3626				0.3581	
White, Non-Hispanic (ref.)								
Black, Non-Hispanic	1.24%	-0.78, 3.26%	0.2296		1.15%	-0.83, 3.14%	0.2554	
Hispanic/Latino	3.01%	-0.28, 6.30%	0.0725		2.77%	-0.45, 5.98%	0.0916	
Other	1.05%	-2.43, 4.54%	0.5528		1.90%	-1.48, 5.29%	0.2704	
Unknown	1.00%	-1.66, 3.65%	0.4616		0.47%	-2.12, 3.06%	0.7227	
Marital Status			0.0001				0.2196	
Married (ref)								
Divorced/Separated	0.09%	-1.60, 1.78%	0.9183		-0.91%	-2.61, 0.80%	0.2971	
Single/Never Married	1.98%	-1.18, 5.14%	0.2189		1.18%	-1.93, 4.29%	0.4553	
Widowed	4.74%	2.62, 6.86%	<0.0001		1.47%	-0.68, 3.61%	0.1796	
% VA Service Connection			<0.0001				<0.0001	
None (ref)								
Less than 50%	-2.93%	-5.10, -0.76%	0.0082		-2.81%	-4.94, -0.68%	0.0097	
50% or more	-8.42%	-9.93, -6.90%	<0.0001		-6.86%	-8.44, -5.28%	<0.0001	
Selim Comorbidity Score			0.0015				0.0003	
0-3 (ref)								
4	2.35%	-0.14, 4.84%	0.0642		4.01%	1.58, 6.45%	0.0012	
5	-1.07%	-3.47, 1.32%	0.3800		1.71%	-0.65, 4.08%	0.1559	
6	-1.99%	-4.43, 0.46%	0.1113		1.90%	-0.56, 4.35%	0.1310	

Variable	Univariable Analysis			Multivariable Analysis		
	Coefficient a	95% CI	p-value	Coefficient a	95% CI	p-value
7	0.46%	-2.18, 3.11%	0.7303	4.91%	2.23, 7.58%	0.0003
8	-2.21%	-4.63, 0.22%	0.0744	4.77%	2.19, 7.34%	0.0003
Major Surgery	-0.92%	-5.24, 3.40%	0.6765	-0.28%	-4.49, 3.92%	0.8955
Baseline Pain Intensity Score						
0 to 4 (ref)						<0.0001
5 to 6	15.32%	13.46, 17.18%	<0.0001	15.65%	13.80, 17.50%	<0.0001
7 to 8	21.85%	19.84, 23.86%	<0.0001	22.43%	20.43, 24.43%	<0.0001
8 to 10	25.03%	21.89, 28.18%	<0.0001	25.72%	22.59, 28.85%	<0.0001
Tobacco Use Disorder	-1.34%	-3.49, 0.82%	0.2235	-0.38%	-2.55, 1.79%	0.7342
Substance Use Disorder	-3.73%	-6.42, -1.05%	0.0065	-2.19%	-4.92, 0.54%	0.1162
Mental Health Disorder	-6.22%	-7.64, -4.81%	<0.0001	-3.99%	-5.50, -2.48%	<0.0001
Rheumatism/Arthritis/Gout	-0.12%	-1.59, 1.35%	0.8700	-2.29%	-3.82, -0.76%	0.0033
Chronic Neck/Joint Pain	0.82%	-0.61, 2.25%	0.2603	0.93%	-0.50, 2.37%	0.2002
Chronic Lower Back Pain	-4.41%	-5.81, -3.01%	<0.0001	-5.06%	-6.47, -3.66%	<0.0001
Other Musculoskeletal Pain	-0.83%	-2.24, 0.58%	0.2477	-0.36%	-1.75, 1.03%	0.6087
Neuropathy	-4.78%	-6.39, -3.16%	<0.0001	-4.19%	-5.78, -2.60%	<0.0001
Headache or Migraine	-1.94%	-4.55, 0.67%	0.1453	-0.53%	-3.07, 2.01%	0.6832
Fibromyalgia/Myofascial Pain	-6.43%	-9.99, -2.86%	0.0004	-4.34%	-7.82, -0.87%	0.0143

^aPositive coefficients represent larger reductions from baseline pain relative to reference group, while negative coefficients represent smaller reductions.

Table 5

Survival Analysis: time to sustained pain improvement from baseline pain intensity scores, N=12,924

Variable	Univariable Analysis			Multivariable Analysis		
	Hazard Ratio	95% CI	p-value	Hazard Ratio	95% CI	p-value
Age			<0.0001			0.1582
65 to 69 years (reference)						
70 to 74	1.07	1.01, 1.14	0.0241	1.01	0.95, 1.07	0.7538
75 to 79	1.13	1.06, 1.20	0.0001	1.04	0.98, 1.11	0.1858
80 to <85	1.20	1.12, 1.29	0.0000	1.08	1.00, 1.16	0.0454
85 or older	1.16	1.07, 1.25	0.0001	1.08	1.00, 1.17	0.0555
Male sex	1.00	0.89, 1.12	0.9821	1.01	0.90, 1.14	0.8362
Race/Ethnicity			0.9581			0.8490
White, Non-Hispanic (ref.)						
Black, Non-Hispanic	1.02	0.96, 1.08	0.5979	1.03	0.96, 1.09	0.4212
Hispanic/Latino	1.02	0.93, 1.13	0.6422	1.03	0.93, 1.14	0.5303
Other	1.02	0.91, 1.13	0.7429	1.05	0.94, 1.17	0.4167
Unknown	1.02	0.94, 1.11	0.5910	1.01	0.92, 1.09	0.8970
Marital Status			0.0102			0.3991
Married (ref)						
Divorced/Separated	0.99	0.94, 1.04	0.6811	0.96	0.91, 1.01	0.1290
Single/Never Married	1.05	0.95, 1.16	0.3113	1.00	0.91, 1.10	0.9867
Widowed	1.10	1.04, 1.18	0.0024	1.01	0.95, 1.08	0.7063
% VA Service Connection			<0.0001			<0.0001
None (ref)						
Less than 50%	0.95	0.89, 1.01	0.1147	0.95	0.89, 1.02	0.1317
50% or more	0.77	0.73, 0.80	<0.0001	0.79	0.75, 0.83	<0.0001
Selim Comorbidity Score			<0.0001			0.2889
0–3 (ref)						
4	1.03	0.95, 1.11	0.4364	1.06	0.98, 1.15	0.1218
5	0.92	0.85, 0.99	0.0268	0.98	0.91, 1.06	0.6585
6	0.89	0.82, 0.96	0.0032	0.98	0.90, 1.06	0.6054

Variable	Univariable Analysis			Multivariable Analysis		
	Hazard Ratio	95% CI	p-value	Hazard Ratio	95% CI	p-value
7	0.90	0.83, 0.98	0.0113	1.01	0.92, 1.10	0.8911
8	0.84	0.78, 0.91	<0.0001	0.99	0.91, 1.08	0.8840
Major Surgery	0.96	0.84, 1.10	0.5675	1.01	0.88, 1.15	0.8955
Baseline Pain Intensity Score			<0.0001			<0.0001
0 to 4 (ref)						
5 to 6	1.26	1.18, 1.33	<0.0001	1.27	1.19, 1.35	<0.0001
7 to 8	1.39	1.30, 1.48	<0.0001	1.42	1.33, 1.51	<0.0001
8 to 10	1.45	1.31, 1.60	<0.0001	1.47	1.33, 1.62	<0.0001
Prior Opioid Prescription ^a	0.71	0.67, 0.76	<0.0001	0.71	0.67, 0.75	<0.0001
Tobacco Use Disorder	0.94	0.87, 1.00	0.0515	0.98	0.91, 1.05	0.5765
Substance Use Disorder	0.83	0.76, 0.91	<0.0001	0.90	0.82, 0.98	0.0190
Mental Health Disorder	0.81	0.78, 0.85	<0.0001	0.89	0.85, 0.93	<0.0001
Rheumatism/Arthritis/Gout	0.98	0.93, 1.02	0.3094	0.96	0.91, 1.01	0.1061
Chronic Neck/Joint Pain	1.01	0.96, 1.05	0.7535	1.03	0.99, 1.08	0.1682
Chronic Lower Back Pain	0.90	0.86, 0.93	<0.0001	0.91	0.87, 0.95	0.0001
Other Musculoskeletal Pain	0.93	0.89, 0.97	0.0011	0.95	0.91, 0.99	0.0153
Neuropathy	0.89	0.84, 0.93	<0.0001	0.91	0.86, 0.95	0.0002
Headache or Migraine	0.96	0.89, 1.04	0.3435	1.00	0.92, 1.09	0.9896
Fibromyalgia/Myofascial Pain	0.79	0.71, 0.89	0.0001	0.82	0.73, 0.93	0.0012

^aTime-varying covariate measuring opioid status (active prescription for opioid medication, yes/no) any time in the follow-up period, up to the month prior to the last month of the 3 month endpoint