




# Real-World Evidence in Prescription Medication Use Among U.S. Adults with Neck Pain

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## ABSTRACT

**Introduction:** Neck pain is a common condition that leads to serious pain, disability, and increased healthcare costs worldwide. Pharmacotherapy is one of the most common strategies to reduce neck pain in patients. The aim of this study was to analyze the real-world pattern of drugs prescribed for patients with neck pain in the USA.

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**Methods:** Data on individuals who reported current neck pain in the 2009–2010 US National Health and Nutrition Examination Survey (NHANES) and with a history of persistent pain for at least 6 weeks or 3 months were extracted from the NHANES database. Those included in the study were divided into three groups based on the duration of pain: the without neck pain group (Group A); subacute group (Group B) with a history of 6 weeks of neck pain; and the chronic neck pain group (Group C) with a history of 3 months of neck pain. The use and duration of medication

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prescribed for Group A, B, and C patients were compared.

**Results:** The analysis revealed that opioid use was significantly more prevalent in the subacute and chronic neck pain group than in the without neck pain group (Group A) (adjusted odds ratio [aOR] 4.20, 95% confidence interval [CI] 2.07–8.52 and aOR 7.00, 95% CI 4.32–11.33, respectively). The factors strongly associated with higher opioid use included older age, low education level, and low family income. In the chronic neck group, opioids, followed in decreasing order of frequency by acetaminophen and nonsteroidal anti-inflammatory drugs, were the most common analgesics used in combination with other analgesics.

**Conclusion:** Our analysis of the data shows that the long-term excessive use of opioids and the underutilization of other analgesics are two major issues in the treatment of neck pain in the USA. Possible improvements include improved education of patients by healthcare professionals on the use of opioids and more consideration given to non-pharmacotherapy options. Our results reveal the potential problem in pharmacotherapy choices for neck pain treatment and may help improve the current clinical practice in the USA and other countries.

**Keywords:** Neck pain; Opioids; Prescription medication; Real-world evidence

### Key Summary Points

#### Why carry out this study?

Neck pain is currently a common condition that leads to serious pain, disability, and increased healthcare costs worldwide.

Pharmacotherapy is one of the most common strategies to reduce neck pain. Information on the pattern of medication use among U.S. adults with neck pain is scarce.

The aim of this study was to analyze the real-world pattern of drugs prescribed for patients with neck pain in the USA.

### What was learned from the study?

Long-term excessive use of opioids and the underutilization of other analgesics are two major issues in the treatment of neck pain in the USA. Older age, low education level, and low family income were found to be strongly associated with more opioid use.

In patients with chronic neck pain, opioids, followed in order of decreasing frequency by acetaminophen and nonsteroidal anti-inflammatory drugs, were the most common analgesics used in combination with other analgesics.

Healthcare professionals should better educate patients on the use of pain medications and consider more non-pharmacotherapy options.

## INTRODUCTION

Neck pain is a common condition that leads to serious pain, disability, and increased healthcare costs worldwide [1–3]. Increasingly more researchers are finding that effective treatment and prevention strategies for neck pain are needed [1, 4]. Pharmacotherapy, including opioids, non-steroidal anti-inflammatory drugs (NSAIDs), and paracetamol, is one of the most common strategies to reduce neck pain reduction in the USA [5, 6]. The U.S. Centers for Disease Control and Prevention released a guideline for prescribing opioids which pointed out that non-pharmacologic therapy and non-opioid pharmacologic therapy should be the preferred treatments for chronic pain [7]. Opioids only should be used after careful consideration and only for short- to medium-term treatment [8]. Previous studies have shown that excessive opioid use for neck pain is very common in the USA [9–12].

The USA has a long history of opioid use and has thereby accumulated a lot of experience in opioid management. This experience could offer important lessons for other countries in

their own efforts to effectively manage opioid use. There is currently a worldwide increase in the demand for prescription opioids, and excessive use of opioids is becoming a serious global problem [13]. Therefore, learning from the USA in terms of managing opioid use is important for other countries [14].

Information on the pattern of medication use among U.S. (i.e., American) adults with neck pain is scarce. Real-world evidence can be helpful in the decision-making process related to therapeutic regimens, drug development, prescribing behavior, patient care, among other factors [15]. However, real-world data on the use patterns of prescription medication for the treatment of neck pain is limited. Therefore, the aim of our study was to analyze the pattern of prescription medication use in neck pain in the USA. Our results also show the demographic characteristics of opioid use in the neck pain population which is helpful for reducing the use of opioids.

## METHODS

### Data Source and Study Participants

Data for this study were collected from the National Health and Nutrition Examination Survey (NHANES) database by a professional statistician. The aim of NHANES is to assess the health and nutritional status of the U.S. adult population [16]. All survey protocols used by the NHANES are evaluated by the National Center for Health Statistics (NCHS) research ethics board and informed consent must be provided [17]. For our study, we used data extracted from the 2009–2010 survey because this survey cycle included a comprehensive neck pain questionnaire administered to participants aged 20–69 years. The neck pain sample was defined as participants in the survey who reported current neck pain at the time of the survey and had a history of persistent pain for at least 6 weeks or 3 months. Participants with cancer, fracture, gout, arthritis (including rheumatoid arthritis, osteoarthritis, psoriatic arthritis, and other arthritis), iritis/uveitis, ulcerative colitis, and Crohn's disease were

excluded from our study, as these conditions might affect the use of analgesics.

The authors of a previous study reported that methadone, buprenorphine, buprenorphine, and naloxone were often used to treat opioid dependence or withdrawal [18]. Therefore, we excluded subjects who use these opioids from our study in order to reduce the impact of opioid dependence on our results.

Participants without neck pain were categorized into Group A ( $n = 3035$ ); those with a history of 6 weeks of neck pain were categorized into Group B ( $n = 158$ ); and participants with a history of 3 months of neck pain were categorized into Group C ( $n = 308$ ). Data extracted from the NHANES database include demographic characteristics (age, sex, race, body mass index [BMI]), education level, annual family income, Patient Health Questionnaire 9 (PHQ9) score, work pattern (vigorous and moderate work), exercise pattern (vigorous and moderate exercise), health conditions (medical comorbidities), extent of pain relief from medications (none, some, most, or all of the pain released) and sleep quality (sleep < 4 h due to pain).

### Use of Prescription Medications

Information on the use of prescription medications was collected during the survey by an interviewer in the participants' homes. The interviewer documented the prescription medications that had been used by the participants within the past 30 days, also requesting to view the prescription bottles, when available, to record the duration of use of each prescription medication. The most common analgesics used for neck pain were found to be opioids, acetaminophen, NSAIDs, salicylates, cyclooxygenase 2 (COX-2) inhibitors, gabapentin, topical lidocaine, muscle relaxants, duloxetine, tricyclic antidepressants, and benzodiazepines. Some anti-depression medications not typically used for pain relief were also identified, including selective serotonin reuptake inhibitors (SSRIs) and non-benzodiazepine hypnotics.

## Statistical Analysis

Groups A, B, and C were compared for the use and duration of prescription medications. Analysis of variance (ANOVA) was used for the comparison of continuous variables and the Chi-square test was used for the comparison of categorical variables.

The characteristics of the participants in Groups A, B, and C were compared by ANOVA for continuous variables and by the Chi-square test for categorical variables. The frequency of the use of various drug combinations was then calculated, and the demographic characteristics of prescription medication use by the participants were determined. Logistic regression was also used to calculate adjusted odds ratios (aOR), which were adjusted for age, race, education level, gender, annual family income, PHQ9 score, and medical comorbidities.

All statistical analyses were conducted using SPSS software version 18 (IBM Corp., Armonk, NY, USA). A *P* value of < 0.05 was considered to indicate statistical significance.

All data were obtained from NHANES directly in de-identified form, and thus this study did not require additional Institutional Review Board (IRB) approval.

## RESULTS

The demographic characteristics of the different groups are shown in Table 1. Women were more likely to develop subacute neck pain (62.0%) and chronic neck pain (58.1%), and patients from low-income families were found to be prone to develop subacute neck pain and chronic neck pain. In addition, patients with subacute and chronic neck pain were more likely to suffer from depression and were had more strenuous work patterns.

The prevalence of prescription medication use among patient with subacute neck pain, chronic neck pain, and no neck pain is shown in Table 2. In the subacute and chronic neck pain groups opioids were the mostly highly used analgesics (7.0 and 12.3% of subjects, respectively) and SSRIs were the mostly used antidepressants drug (9.5 and 12.3%,

respectively). Opioid use was significantly more prevalent in the subacute and chronic neck pain group than in the no-neck pain group (aOR 4.20, 95% confidence interval [CI] 2.07–8.52 and aOR 7.00, 95% CI 4.32–11.33, respectively). The use of acetaminophen, NSAIDs, muscle relaxants, and gabapentin was much more common in the chronic neck pain group than in the no-neck pain group (aOR 6.44, 95% CI 4.02–10.30; aOR 4.63, 95% CI 2.91–7.37; aOR 7.66, 95% CI 3.90–15.06; aOR: 8.88, 95% CI 3.62–21.77, respectively). In addition, duloxetine and COX-2 inhibitors were also medications of preference by chronic neck pain patients (aOR 4.02, 95% CI 1.52–10.60 and aOR 5.06, 95% CI 1.59–16.09, respectively). However, tricyclic antidepressants and topical lidocaine were rarely used by both groups. The prevalence of hypnotics was also higher in subacute and chronic neck pain patients than in those without neck pain (7.6 and 5.8%, respectively).

Analysis of the median duration of prescription medication use revealed that the duration of opioid use was significantly longer in the subacute and chronic neck pain groups (mean duration 243 and 395 days, respectively) than in the non-neck pain group (mean duration 36 days) (Table 3). In the chronic neck pain group, the median duration of acetaminophen and NSAID use was 1095 and 319 days, respectively.

The frequency of various drug combinations used by the chronic neck pain population is shown in Fig. 1. Opioids, followed in decreasing order of frequency by acetaminophen, NSAIDs, and muscle relaxants, were the most common analgesics combined with other analgesics. The most common combination used by the chronic neck pain population was opioids with acetaminophen or NSAIDs (3.6%). Other common combinations include opioids with muscle relaxants, SSRIs, benzodiazepines, or hypnotics (2.3%) and opioids with gabapentin (1.60%).

Subgroup analysis by demographic characteristics was conducted for the chronic neck pain group (Fig. 2). Opioid use in the chronic neck pain population was found to be most common among patients aged > 60 years (21.7%), non-Hispanic blacks (16.5%), those

**Table 1** Demographic and behavioral characteristics of the American adults aged 20–69 years with no neck pain, subacute neck pain, and chronic neck pain

Demographic and behavioral characteristics	Study patient groups			<i>P</i> value
	Group A: without neck pain ( <i>n</i> = 3035)	Group B: with subacute neck pain ( <i>n</i> = 158)	Group C: with chronic neck pain ( <i>n</i> = 308)	
Age (years)	43.43 ± 16.14	42.09 ± 13.94	45.85 ± 12.03	< 0.001
BMI ( kg/m <sup>2</sup> )	28.60 ± 6.39	27.72 ± 8.29	28.87 ± 7.56	0.194
Gender				< 0.001
Male	1580 (52.1%)	60 (38.0%)	129 (41.9%)	
Female	1455 (47.9%)	98 (62.0%)	179 (58.1%)	
Race				0.667
Non-Hispanic White	1501 (49.5%)	81 (51.3%)	141 (45.8%)	
Non-Hispanic Black	544 (17.9%)	24 (15.2%)	53 (17.2%)	
Mexican American	565 (18.6%)	28 (17.7%)	57 (18.5%)	
Other Hispanic	279 (9.2%)	16 (10.1%)	37 (12.0%)	
Other race—including multi-racial	146 (4.8%)	9 (5.7%)	20 (6.5%)	
Education				0.326
College and higher	671 (22.1%)	31 (19.6%)	53 (17.2%)	
High school/Associate's degree	1570 (51.7%)	83 (52.5%)	173 (56.2%)	
Less than high school	794 (26.2%)	44 (27.8%)	82 (26.6%)	
Annual family income (US\$)				0.066
> 100,000	444 (14.6%)	18 (11.4%)	27 (8.8%)	
65–99,000	409 (13.5%)	20 (12.7%)	39 (12.7%)	
45–64,000	408 (13.4%)	20 (12.7%)	41 (13.3%)	
20–44,000	1026 (33.8%)	51 (32.3%)	105 (34.1%)	
< 20,000	748 (24.6%)	49 (31.0%)	96 (31.2%)	
PHQ9 score (depression)				< 0.001
0–4 (non-depression)	2306 (76.0%)	100 (63.3%)	162 (52.6%)	
5–9 (mild depression)	487 (16.0%)	29 (18.4%)	68 (22.1%)	
10–14 (moderate depression)	163 (5.4%)	12 (7.6%)	37 (12.0%)	
15–19 (moderate–severe depression)	54 (1.8%)	12 (7.6%)	27 (8.8%)	
20–27 (severe depression)	25 (0.8%)	5 (3.2%)	14 (4.5%)	

**Table 1** continued

Demographic and behavioral characteristics	Study patient groups			P value
	Group A: without neck pain (n = 3035)	Group B: with subacute neck pain (n = 158)	Group C: with chronic neck pain (n = 308)	
Work pattern				
Vigorous work	601 (19.8%)	49 (31.0%)	72 (23.4%)	< 0.001
Vigorous work time (minutes/day)	201.73 ± 426.12	216.02 ± 198.19	222.46 ± 160.09	0.897
Moderate work	1149 (37.9%)	66 (41.8%)	130 (42.2%)	0.221
Moderate work time (minutes/day)	166.04 ± 319.82	157.27 ± 128.90	158.57 ± 136.03	0.943
Reaction exercise				
Vigorous reaction exercise	723 (23.8%)	35 (22.2%)	48 (15.6%)	< 0.01
Vigorous reaction exercise time (minutes/day)	79.11 ± 59.09	73.86 ± 63.24	75.63 ± 43.20	0.816
Moderate reaction exercise	1275 (42.0%)	65 (41.1%)	107 (34.7%)	0.180
Moderate reaction exercise time (minutes/day)	67.57 ± 57.16	58.46 ± 62.36	61.79 ± 59.65	0.302
Medical comorbidities				
0–1	2462 (81.1%)	98 (62.0%)	191 (62.0%)	< 0.001
2–3	521 (17.2%)	52 (32.9%)	96 (31.2%)	
> 3	52 (1.7%)	8 (5.1%)	21 (6.8%)	

Values in table are given as the mean ± standard deviation (SD) or as a number with the percentage in parenthesis  
*BMI* Body mass index, *PHQ9* Patient Health Questionnaire 9

with a annual family income lower < US\$ 20,000 (13.8%), and those with a lower education level (10.9% among those with a GED/AA degree [GED/AA is equivalent to a high school diploma] and 16.7% among those with less than high school education compared with 4% use among those with a college degree and higher). In addition, patients of older age and those with a lower education level, as well as female patients, were more likely to use acetaminophen and NSAIDs. Subsequent analysis of the risk factors for chronic neck pain patients to use opioids, NSAIDs, and muscle relaxants revealed that older age, lower education level,

and lower family income were strongly associated with increased opioid use. We also found that male patients and patients with more comorbidities (> 3) were more likely to use acetaminophen for pain relief and that patients with depression were more likely to use NSAIDs. However, age, education level, and family income did not affect the use of acetaminophen, NSAIDs, and muscle relaxants: the aOR (95% CI) was 2.27 (1.02–5.19) for the GED/AA degree group and 4.12 (1.40–12.1) for those with less than a high school education compared with those with a college degree or higher (Table 4).

**Table 2** Prescription medication use among the American adult participants

Prescription medications	Study patient groups			P value	aOR <sup>a</sup> (95% CI)	aOR <sup>a</sup> P value	aOR <sup>b</sup> (95% CI)	aOR <sup>b</sup> P value
	Group A: without neck pain (n = 3035)	Group B: with subacute neck pain (n = 158)	Group C: with chronic neck pain (n = 308)					
Pain-related medications								
Opioids	45 (1.5%)	11 (7.0%)	38 (12.3%)	< 0.001	4.20 (2.07–8.52)	< 0.001	7.00 (4.32–11.33)	< 0.001
Acetaminophen	54 (1.8%)	11 (7.0%)	35 (11.4%)	< 0.001	3.74 (1.88–7.44)	< 0.001	6.44 (4.02–10.30)	< 0.001
NSAIDs	62 (2.0%)	13 (8.2%)	34 (11.0%)	< 0.001	3.61 (1.90–6.88)	< 0.001	4.63 (2.91–7.37)	< 0.001
Muscle relaxants	22 (0.7%)	4 (2.5%)	18 (5.8%)	< 0.001	3.43 (1.14–10.31)	0.028	7.66 (3.90–15.06)	< 0.001
Gabapentin	12 (0.4%)	2 (1.3%)	12 (3.9%)	< 0.001	3.17 (0.67–15.06)	0.147	8.88 (3.62–21.77)	< 0.001
Benzodiazepines	40 (1.3%)	9 (5.7%)	19 (6.2%)	< 0.001	2.80 (1.27–6.19)	0.011	2.70 (1.46–4.98)	0.002
Salicylates	41 (1.4%)	2 (1.3%)	8 (2.6%)	0.216	0.87 (0.20–3.88)	0.86	1.47 (0.62–3.48)	0.384
Duloxetine	15 (0.5%)	3 (1.9%)	7 (2.3%)	0.001	3.57 (0.98–13.00)	0.053	4.02 (1.52–10.60)	0.005
Tricyclic antidepressants	14 (0.5%)	3 (1.9%)	5 (1.6%)	0.006	2.89 (0.77–10.83)	0.115	2.45 (0.81–7.42)	0.113
COX2 inhibitors	8 (0.3%)	1 (0.6%)	6 (1.9%)	< 0.001	1.85 (0.22–15.76)	0.574	5.06 (1.59–16.09)	0.006
Topical lidocaine	2 (0.1%)	0 (0)	2 (0.6%)	0.014	–	–	12.01 (1.54–93.76)	0.018
Non-pain antidepressants								

Table 2 continued

Prescription medications	Study patient groups		P value	aOR <sup>a</sup> (95% CI)	aOR <sup>a</sup> P value	aOR <sup>b</sup> (95% CI)	aOR <sup>b</sup> P value
	Group A: without neck pain (n = 3035)	Group B: with subacute neck pain (n = 158)					
SSRI	103 (3.4%)	15 (9.5%)	38 (12.3%)	5.08 (1.13–3.80)	0.018	2.55 (1.66–3.92)	< 0.001
Other non-pain antidepressants	55 (1.8%)	3 (1.9%)	15 (4.9%)	0.53 (0.16–1.80)	0.307	1.37 (0.72–2.63)	0.337
Hypnotics	31 (1.0%)	12 (7.6%)	18 (5.8%)	6.30 (3.05–13.02)	< 0.001	4.10 (1.17–7.76)	< 0.001

Values for study groups are presented as the number (of patients) with the percentage in parenthesis

aOR Adjusted odds ratio, adjusted for age, race, gender, education, family income, depression score and medical comorbidities, CI confidence interval, COX2 cyclooxygenase 2, SSRI selective serotonin reuptake inhibitor, NSAIDs nonsteroidal anti-inflammatory drugs

<sup>a</sup> aOR is for subacute neck pain population

<sup>b</sup> aOR is for chronic neck pain population



**Table 3** Self-reported duration of prescription medication use

Prescription medications	Median number of days (IQR) of medication use in subjects without neck pain (Group A, n = 3035)	Median number of days (IQR) of medication use in subjects with subacute neck pain (Group B, n = 158)	Median number of days (IQR) of medication use in subjects with chronic neck pain (Group C, n = 308)	P value
<b>Pain-related medications</b>				
Opioids	36 (10.50–121)	243 (182–874)	395 (205–1825)	< 0.001
Acetaminophen	25 (6.5–319.25)	61 (14–365)	1095 (365–1825)	< 0.001
NSAIDs	45.50 (12.50–235.75)	730 (17.50–1460.00)	319 (61.00–1460.00)	< 0.001
Muscle relaxants	41 (5–365)	547 (94.25–1277.50)	456 (304.25–730.00)	< 0.001
Gabapentin	730 (129.50–1003.75)	912.5 (730–NR)	365 (182–1551.25)	0.807
Benzodiazepines	730 (296.75–3650)	122 (76–1277.50)	730 (182.0–2555.0)	0.321
Salicylates	1095 (365.0–2372.50)	2920 (1460–NR)	1095 (243–2463.75)	0.884
Duloxetine	730 (182–1095)	547 (730–NR)	1460 (243–2190)	0.301
Tricyclic antidepressants	912.50 (365.0–4653.75)	1460 (14–NR)	912 (638.50–2190)	0.543
COX-2 inhibitors	395.50 (37.75–3102.50)	1825 (1825–1825)	136 (13–1277)	0.749
Topical lidocaine	1825 (1460–NR)	NA	760.50 (61–NR)	0.310
<b>Non-pain-related antidepressants</b>				
SSRI	730 (243–1825)	1095 (365–2555)	1277 (182–2646)	0.708
Others	365 (213–1460)	1095 (30–NR)	1825 (365–2920)	0.324
Hypnotics	365 (91–1460)	547.50 (182.75–1368.75)	365 (83.50–2007.50)	0.591

P values obtained for log-transformed values  
 IQR Interquartile range, NA not applicable, NR not reached

The efficacy of analgesics (Table 5) was also assessed. According to the self-report of the subjects, there was no significant difference between opioids and other commonly used analgesics ( $P > 0.05$ ). In terms of life quality improvement, there was also no significant difference between opioids and other commonly used analgesics in terms of pain reduction, with the result being insomnia ( $P > 0.05$ ). However, the results did reveal that NSAIDs had were more efficacious than acetaminophen for pain relief.

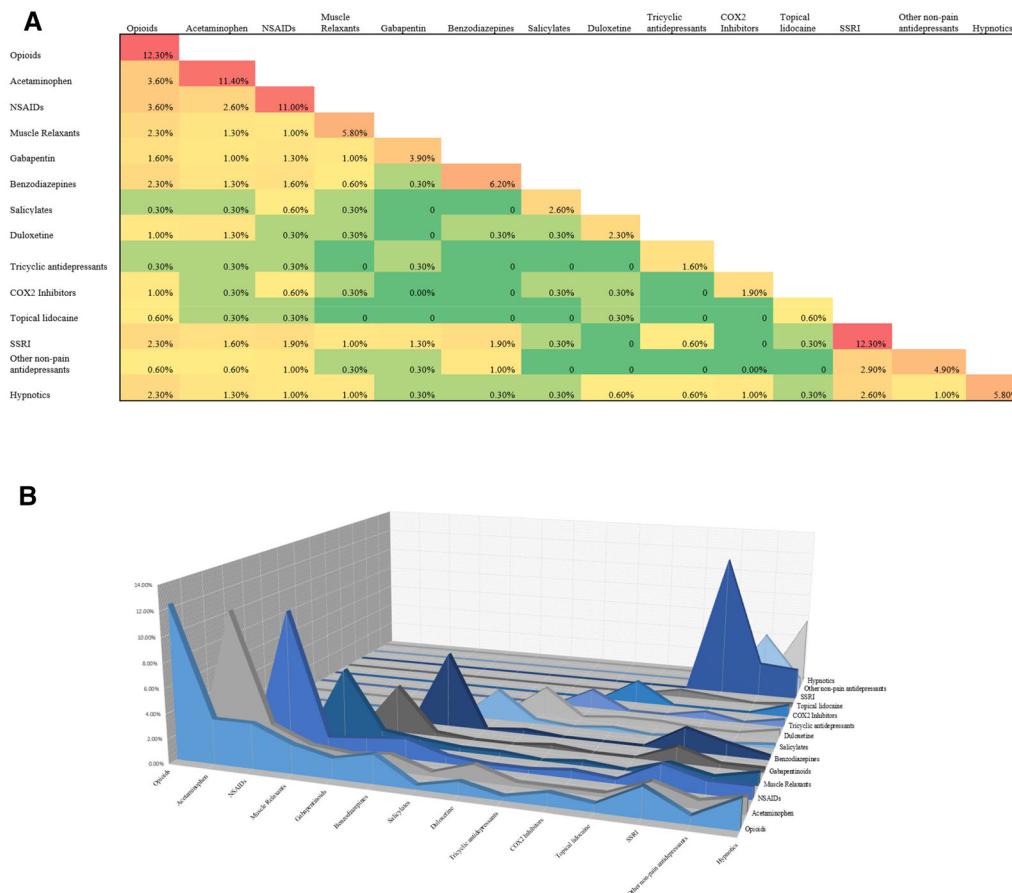
## DISCUSSION

The aim of our study was to analyze the use of different prescription analgesics by U.S. adults with neck pain using real-world data. We found that opioids were the most common analgesics used for pain management by patients with neck pain and that they were used for a relatively longer time compared to other common analgesics. Previous studies have shown that during recent decades excessive use of opioid analgesics has been and still is a common and serious problem in the USA [19–21]. Although many professional medical societies have made appeals to reduce the use of opioids, the level of opioid use in the USA remains fourfold higher than the current prescription rate in Europe and threefold higher than it was 1999 [19, 22, 23]. Studies have demonstrated that the effect of oral opioids is not superior to that of NSAIDs in terms of reducing non-cancer pain in the short term [24, 25]. Meredith et al. pointed out that there was no evidence of any long-term benefits of opioids in terms of reducing chronic non-cancer pain [26]. In addition, opioids can lead to many adverse events, such as fractures, myocardial infarction, abuse, and opioid-induced hyperalgesia and tolerance [27, 28]. The conclusion to be drawn from these studies is that opioids do not have the desired effect in reducing pain, but they do increase the risk of adverse events.

Earlier studies showed that there was a significant decrease in opioid use by patients with low back, neck, knee, and shoulder pain between 2008 and 2014 in the USA [29].

However, the extent of this decrease was not significant among patients with neck pain [29]. Machado et al. pointed out that there have been very few trials aimed at showing the effectiveness of NSAIDs on neck pain [30]. In one study, Peloso et al. showed that there was limited and unclear evidence the NSAIDs were effective in reducing neck pain [31]. However, despite the high incidence of neck pain were, there is still insufficient evidence to support specific interventions for conservative treatments [32–34]. Therefore, one possible explanation of why the extent of the decrease in opioid use was not significant among neck pain populations may be that there is a lack (or limited number) of high-quality trials demonstrating the effectiveness of non-opioid therapies [35]. Lin et al. noted that recent clinical guidelines universally recommend psychosocial assessment for musculoskeletal pain, with the exception of neck pain [36]. Psychological states have been shown to be significantly associated with the extent of opioid abuse [37, 38]. However, recommendations based on psychological status assessment of neck pain treatment have been contradictory, showing that the effect of psychological status in neck pain patients is not well understood. It has been pointed out that psychotherapy could reduce the risk of opioid misuse among chronic pain patients [39]. Based on all of these studies, it is possible that an underestimation of psychological factors may be another reason why patients with neck pain show an extended use of opioids. Consistent with the results reported by Friedman et al. [42], we found that in the USA low-income patients were more likely to use opioids [40]. Gangavalli et al. pointed out that low-income patients believe that they are not prescribed enough pain medications, including opioids [41]. Other factors also contribute to this result, including (1) unmeasured patient-level characteristics; (2) doctors' prescribing practices in low-income neighborhoods; (3) low-income patients not questioning the appropriateness of prolonged opioid treatment [42].

Opioid use and the use of other analgesics in combination with opioids increase with pain impact levels [9, 43, 44]. One study showed that early physical therapy for neck pain may



**Fig. 1** Combinations of different medications used by U.S. adults with chronic neck pain. **a** Heat map, **b** area graph. **a** The most frequently co-administered medications are given in red and the least frequently co-administered medications are given in green. Note that some subjects

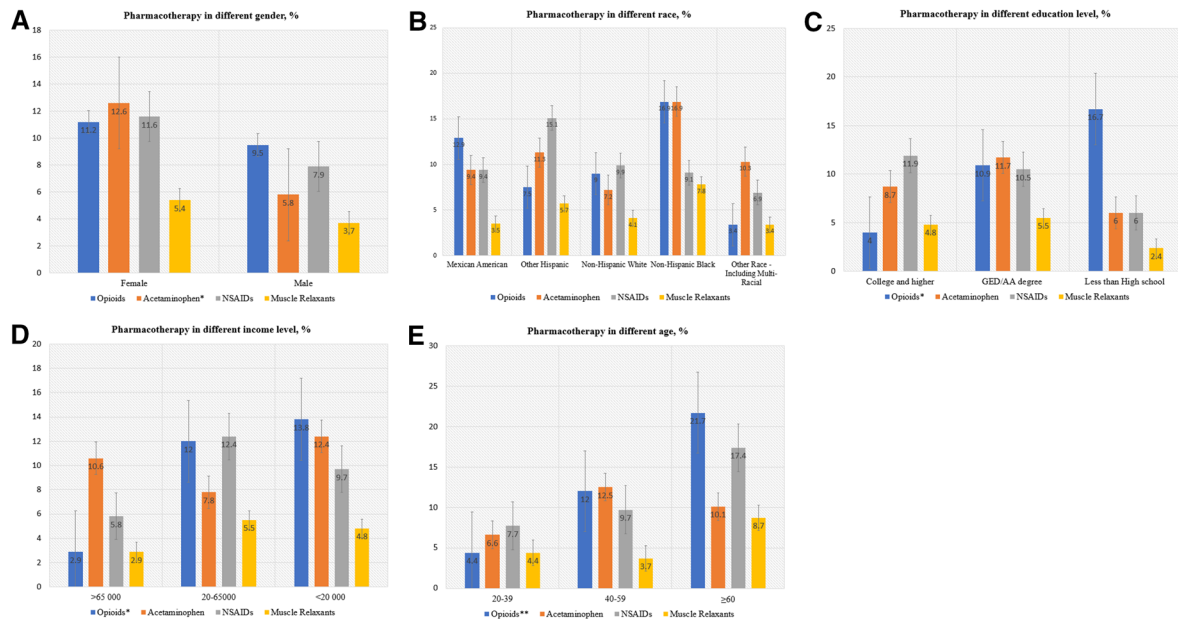
used more than two classes of medications at the same time. *COX2* Cyclooxygenase 2, *NSAIDs* nonsteroidal anti-inflammatory drugs, *SSRI* selective serotonin reuptake inhibitor

decrease total treatment costs and the use of prescription medicines, including opioids [45]. The authors of another study reported that early physical therapy may reduce both the frequency and level of opioid use for all of the musculoskeletal pain regions [46]. The conclusion to be drawn here is that early physical therapy or exercise therapy may be a good option to reduce the use of opioids and/or other analgesics when the pain level remains low.

Weeks et al. pointed out that patients with neck pain who use opioids are more likely to use pain medications and benzodiazepines [12]. This is similar to our results, which show that opioids are the most common analgesics that are used in combination with other analgesics.

Some combinations of medications may prolong the treatment effect and reduce opioid requirements [47]. However, the combination may also contribute to drug overdose when other analgesics are combined with opioids, thus increasing the risk of visits to the emergency department [48]. Therefore, it may be worth changing treatment preferences to reduce the initial use of opioids.

Our analysis also revealed that patients with lower education levels and from low-income families were more likely to use opioids for managing their neck pain. One possible explanation is that these populations are overly dependent on medications and that they lack an understanding of the exact effect of opioids



**Fig. 2** Demographic distribution of pain medication use in U.S. adults with chronic neck pain. The bar charts illustrate the distribution of pain medication use in the chronic neck pain population by age (a), gender (b), race (c), family income (d), and education level (e). *GED/AA*

General educational development and Associate's degree (equivalent to high school diploma). Chi-square \* $p < 0.05$ ; \*\* $p < 0.01$

as well as their serious side effects. All recent guidelines for neck pain treatment recommend patient education programs, such as encouraging patients to return to normal activities as soon as possible, minimizing use of a cervical collar, and performing postural and mobility exercises, and non-pharmaceutical therapy before initiating a patient on pharmacotherapy [49–51]. Thus, healthcare professionals should encourage health education, especially for the patient populations mentioned above, and recommend non-pharmaceutical therapy, including exercise, manual therapy, and psychological therapy, as the first-line treatment. Takaki et al. reported that tobacco users were more likely than non-users to use opioid analgesics in combination with/without muscle relaxants and/or benzodiazepines for non-cancer pain [52]. Thus, healthcare professionals also should consider limiting opioid use by tobacco users.

Our results suggest that healthcare professionals should pay more attention to reducing opioid use in the neck pain population in

general. However, there are issues to be addressed. First, in terms of the whole country, especially in low-income neighborhoods, doctors should unify and standardize treatment strategies. Second, a patient's socioeconomic background, such as education level and income, are crucial factors to be taken into consideration when choosing pharmacotherapy, and as such should be considered in the development of the clinical guideline. Third, doctors should make an extra effort to educate patients on the appropriate pain management strategies.

Regarding analgesic efficacy, we found that opioids were not more effective than acetaminophen or NSAIDs in terms of pain relief. This result is consistent with those of previous studies [53–55]. Drug overdose has been estimated to have caused 10,000–20,000 deaths in the USA; as well, the many other adverse effects of opioids need to be considered [56, 57]. Although acetaminophen and NSAIDs also have some limitations, such as cardiovascular and

**Table 4** Adjusted odds ratio of demographic factors associated with pain medication use in U.S. adults with neck pain

Demographic factors	Adjusted odds ratio (95% CI)			
	Opioids	Acetaminophen	NSAIDs	Muscle relaxants
Age	1.05 (1.02–1.08)**	1.01 (0.98–1.04)	1.02 (0.99–1.04)	1.02 (0.99–1.06)
Gender				
Female	REF	REF	REF	REF
Male	0.87 (0.44–1.71)	0.45 (0.22–0.91)*	0.77 (0.39–1.51)	0.72 (0.28–1.84)
Race				
Mexican American	REF	REF	REF	REF
Other Hispanic	0.36 (0.10–1.35)	1.17 (0.37–3.73)	1.40 (0.47–4.17)	1.50 (0.28–7.96)
Non-Hispanic white	0.66 (0.28–1.57)	0.79 (0.32–1.96)	1.00 (0.42–2.41)	1.13 (0.30–4.34)
Non-Hispanic black	1.31 (0.49–3.50)	2.01 (0.75–5.35)	0.87 (0.29–2.62)	2.02 (0.48–8.63)
Other race—including multi-racial	0.33 (0.04–2.88)	1.25 (0.30–5.24)	0.67 (0.13–3.57)	1.02 (0.10–10.54)
Education				
College and higher	REF	REF	REF	REF
GED/AA degree	2.27 (1.02–5.19)*	1.51 (0.70–3.26)	0.96 (0.47–1.95)	1.26 (0.45–3.51)
Less than high school	4.12 (1.40–12.1)*	0.75 (0.24–2.41)	0.59 (0.19–1.77)	0.60 (0.11–3.27)
Annual family income (US\$)				
> 65,000	REF	REF	REF	REF
20–65,000	5.40 (1.52–19.22)**	0.60 (0.26–1.39)	1.86 (0.72–4.79)	1.71 (0.46–6.43)
< 20,000	5.88 (1.55–22.25)*	0.98 (0.41–2.37)	1.12 (0.39–3.25)	1.42 (0.33–6.16)
Medical comorbidities				
0–1	REF	REF	REF	REF
2–3	0.86 (0.41–1.82)	1.46 (0.74–2.90)	1.78 (0.91–3.46)	1.64 (0.65–4.14)
> 3	3.58 (1.30–9.89)*	2.28 (0.72–7.24)*	1.18 (0.35–4.06)	0.73 (0.08–6.43)
PHQ9 score (depression)	1.04 (0.99–1.08)	0.99 (0.95–1.04)	1.05 (1.01–1.09)*	0.99 (0.92–1.06)

GED/AA General educational development and Associate's degree (equivalent to high school diploma), REF reference  
\* $P < 0.05$ ; \*\* $P < 0.01$

renal toxicity, hypertension, and gastrointestinal damage, restrictions to the use of step 3 analgesics (i.e. strong-acting opioids) in patients with non-cancer pain is urgent [58]. However, if other analgesics are truly ineffective, it remains legitimate and even advisable to use opioids for short periods (< 3 months) [59]. We also found that the NSAIDs were more efficacious than

acetaminophen in terms of neck pain relief. Previous studies also pointed out that acetaminophen has a very small analgesic effect when compared with NSAIDs in musculoskeletal diseases, while acetaminophen has similar side effects with NSAIDs [60, 61]. In our study, we found the usage of COX-2 inhibitors remains low among patients with neck pain

**Table 5** Adjusted odds ratio of different analgesics for pain relief and improved life quality

Models of pain relief	Pain relief			Quality of life				
	Some pain relief <sup>a</sup> (95% CI)	P value	Most pain relief <sup>b</sup> (95% CI)	P value	Sleep < 4 h due to pain (95% CI)	P value	Pain response to exercise (95% CI)	P value
Model 1								
Opioids only	REF	REF	REF	REF	REF	REF	REF	REF
Acetaminophen only	0.49 (0.08–2.88)	0.431	0.23 (0.03–1.66)	0.146	0.08 (0.003–1.94)	0.12	0.67 (0.12–3.72)	0.646
NSAIDs only	3.53 (0.40–30.84)	0.255	2.66 (0.46–15.54)	0.277	0.56 (0.04–7.21)	0.654	0.57 (0.11–3.00)	0.511
Muscle relaxants only	0.75 (0.05–12.47)	0.84	1.14 (0.06–21.70)	0.932	NA	NA	6.21 (0.35–110.91)	0.214
Model 2								
Acetaminophen only	REF	REF	REF	REF	REF	REF	REF	REF
Opioids only	1.65 (0.32–8.55)	0.553	2.27 (0.39–13.12)	0.359	5.51 (0.38–80.63)	0.212	2.01 (0.38–10.67)	0.41
NSAIDs only	7.29 (1.09–48.81)	0.41	10.94 (2.08–57.65)	0.005	7.47 (0.40–138.60)	0.177	0.86 (0.20–3.67)	0.83
Muscle relaxants only	1.55 (0.11–22.28)	0.749	4.81 (0.28–82.64)	0.279	NA	NA	9.68 (0.53–176.39)	0.13

*aOR* Adjusted odds ratio, adjusted for age, race, gender, education, family income, depression score and medical comorbidities

<sup>a</sup> Some, most, and all pain relief vs. no pain relief

<sup>b</sup> Most and all pain relief vs. no pain relief

patients. However, COX-2 inhibitors have similar analgesic effects as traditional NSAIDs but with lower gastrointestinal and cardiovascular toxicity [61, 62]. Therefore, COX-2 inhibitors may be a promising pharmacotherapy for the management of musculoskeletal pain. However, more clinical trials in this area and relative clinical guidelines are needed.

Our study is based on real-world data and shows the specific prescription medication use pattern among U.S. adults with neck pain. Our results reveal the potential problem in pharmacotherapy choices for neck pain treatment and may help improve the current clinical practice in the USA and other countries.

### Limitations

There are a number of limitations to this study. First, our data included some self-reported variables which may lead to measurement error and recall bias. Second, the specific dosage and frequency of each prescription medication could not be evaluated, which impedes further study of the rate of drug abuse because the database does not provide these data. Third, some of the participants may have concealed their medication history, and thus the use of some of the medications may be underestimated. Lastly, it is not clear if the analgesics were used only for neck pain, which may lead to an overestimation of the usage rate of prescription medications.

### CONCLUSION

Previous studies have shown that excessive long-term use of opioids and underutilization of other analgesics are two major issues in the treatment of neck pain in the USA. In our study, patients with a lower education level and low family income were more likely to use opioids to reduce neck pain. Possible improvements could be better patient education by healthcare professionals on the use of opioids and more consideration given to non-pharmacotherapy options to reduce opioid dependence and the related side effects of opioids as recommended by recent guidelines. Our results reveal the

potential problem in pharmacotherapy choices for neck pain treatment and may help improve the current clinical practice in America and other countries.

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Yan Michael Li and Ai-Min Wu have nothing to disclose.

**Compliance with Ethics Guidelines.** All data were obtained from NHANES directly in de-identified form, and thus this study did not require additional Institutional Review Board approval.

**Data Availability.** The datasets generated during and analyzed during the current study are available in the National Health and Nutrition Examination Survey (NHANES), <https://www.cdc.gov/nchs/nhanes/index.htm>.

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