Osteoarthritis and Cartilage 27 (2019) 1018–1025

Osteoarthritis and Cartilage

Social & psychological factors associated with oral analgesic use in knee osteoarthritis management

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ARTICLE INFO

Article history:
Received 21 August 2018
Accepted 23 January 2019

Keywords:
Osteoarthritis
Treatment
Utilization
Depression
Social support
Health literacy

SUMMARY

Objective: Determine modifiable social and psychological health factors that are associated with use of oral opioid and non-opioid medications for OA.
Methods: Patients were categorized based on use of the following oral medications: opioids (with/without other oral analgesic treatments), non-opioid analgesics, and no oral analgesic treatment. We used multinomial logistic regression models to estimate adjusted relative risk ratios (RRRs) of using an opioid or a non-opioid analgesic (vs. no oral analgesic treatment), comparing patients by levels of social support (Medical Outcomes Study scale), health literacy ("How confident are you filling out medical forms by yourself?"), and depressive symptoms (Patient Health Questionnaire-8). Models were adjusted for demographic and clinical characteristics.
Results: In this sample (mean age 64.2 years, 23.6% women), 30.6% ($n = 110$) reported taking opioid analgesics for OA, 54.2% ($n = 195$) reported non-opioid use, and 15.3% ($n = 55$) reported no oral analgesic use. Opioid users had lower mean social support scores (10.0 vs 10.5 vs 11.9, $P = 0.007$) and were more likely to have moderate-severe depressive symptoms (42.7% vs 24.1% vs 14.5%, $P < 0.001$). Health literacy did not differ by treatment group type. Having moderate-severe depression was associated with higher risk of opioid analgesic use compared to no oral analgesic use (RRR 2.96, 95%CI 1.08–8.07) when adjusted for sociodemographic and clinical factors. Neither social support nor health literacy was associated with opioid or non-opioid oral analgesic use in fully adjusted models.
Conclusions: Knee OA patients with more severe depression symptoms, compared to those without, were more likely to report using opioid analgesics for OA.

Introduction

The American College of Rheumatology (ACR), the Osteoarthritis Research Society International (OARSI), and other professional organizations have developed recommendations for the management of knee OA.[1,2] Oral pharmacologic therapies are recommended for the initial management of patients with knee OA, including acetaminophen, non-steroidal anti-inflammatory drugs (NSAIDs), and cyclooxygenase-2 (COX-2) selective inhibitors. Opioid analgesics are also recommended in patients who have failed conservative medical therapy and in patients unwilling to undergo or have contraindications for joint replacement surgery.

These ACR- and OARSI- recommended treatments are based on the "best available evidence" of benefit and safety of pharmacologic agents and the consensus of clinical experts from a wide range of disciplines.[1,2] However, both also acknowledge that these

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https://doi.org/10.1016/j.joca.2019.01.010
1063-4584/

medications are associated with certain adverse effects. For instance, there are concerns about iatrogenic opioid addiction, opioid-induced hyperalgesia, and opioid-induced decreases in quality of life.[3] OA management may need to be tailored based on patients' medical history, comorbidities, social history, and treatment preferences.

Identifying the determinants of OA pharmacologic treatment use may allow better understanding of how patients may choose among the various oral pharmacologic options for knee OA. Traditional models of health service utilization typically include what Andersen has termed "predisposing," "enabling," and "need" factors as determinants of treatment use (Fig. 1).[4] Predisposing factors include biological factors that increase the likelihood of needing care, social statuses that influence individuals' access to care and ability to cope (e.g., education, income), and people's health beliefs. Enabling factors facilitate access to services (e.g., health insurance coverage). Need factors refer to the unpleasantness of individuals' symptoms and beliefs about the causes and seriousness of symptoms. Previous OA studies have examined many of these determinants of OA treatment use. Younger age,[5–7] female sex,[6,8–11] higher educational attainment,[5,7,9] having medical insurance,[9] greater OA disease severity,[5–7,11] and higher number of comorbidities[7–9] have all been associated with increased use of various oral pharmacologic treatments for OA.

Despite the number of factors that are identified in Andersen's model of medical service/treatment utilization, the model has generally overlooked the important effects of individuals' social and psychological health.[4,12] These health factors may influence perceptions of need and use of medical treatments. The extent and quality of social relationships can serve as an enabling resource to facilitate or impede use of treatments.[4,13–15] In a cohort of primary care patients with OA, though, having low level of social support was strongly associated with increased clinic visits that may translate to more receipt of medication prescriptions.[16] Psychological characteristics considered as predisposing variables to use of treatments include cognitive impairment[4,17] and mood disorders, such as depression and anxiety.[18–21] Arthritis patients with limited health literacy may make greater use of health services and treatments designed to treat (rather than prevent) disease complications, including analgesic medications.[22] A literature review concluded that OA patients with anxiety and depression took more analgesic medications than other OA patients without these comorbidities.[23] The association of these social and psychological health factors with the utilization of an oral opioid agent instead of a non-opioid analgesic or no oral analgesic treatment at all for OA is unknown, however.

Of utmost importance, while many of the known determinants of OA treatment use are relatively fixed, several social and psychological health factors are modifiable at the point of care.[24] Quality of social relationships, psychological/personality dispositions, and other psychosocial risk factors may all be targeted.[24,25] Health literacy can be improved through provision of information, effective communication, and structured education.[26] The primary objective of this study was to determine which potentially modifiable social and psychological health factors are associated with use of various oral analgesic treatments in a sample of patients with chronic knee pain due to OA. We hypothesized that lower levels of social support, inadequate health literacy, and higher levels of depression would all be associated with increased use of opioid analgesic vs non-opioid and no oral analgesic treatment use.

Methods

Study design and setting

This study is a cross-sectional analysis of baseline data from a clinical trial. The study sample includes participants of a clinical trial of a positive psychological intervention on pain among individuals with symptomatic knee OA recruited from two large, urban, academic Veterans Affairs (VA) medical centers.[27] Details of the study design and protocol have been described previously.[27] Briefly, 180 African American and 180 white primary care patients with chronic pain from knee OA were randomized to a 6-week program of either positive psychological skill building-activities or neutral control activities. Patients who met study criteria were invited to complete a baseline questionnaire administered by trained research staff. The study was approved by the VA Central Institutional Review Board.

Participants

Patients who met the following criteria based on a review of VA electronic medical records were mailed an invitation to be screened for the study: non-deceased; non-Hispanic African American or white race; 50 years or older; had a primary care visit at a participating site in the past 12 months; had a diagnosis of OA

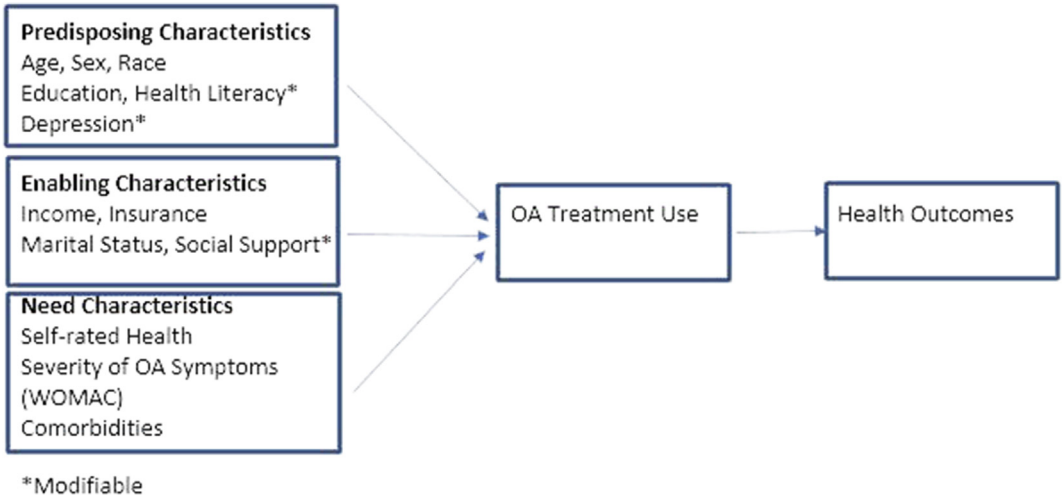

Fig. 1. Behavioral model for OA oral analgesic treatment use. Abbreviations; OA, osteoarthritis; WOMAC, Western Ontario & McMaster Universities Osteoarthritis Index.

(International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM] code 715); and did not have a diagnosis of a rheumatologic disease associated with inflammatory arthritis (rheumatoid arthritis, lupus, psoriatic arthritis, or ankylosing spondylitis) or Alzheimer's disease/dementia based on ICD-9-CM codes. Patients who expressed interest or did not respond within 2 weeks were called over the telephone by research staff to determine study eligibility prior to enrollment.

Individuals were included in the study if they were ≥50 years of age; received primary care at a participating site; self-reported as non-Hispanic African American or white; had frequent pain characteristic of symptomatic knee OA identified using questions from the Osteoarthritis Initiative study;[28] rated their pain ≥4 on a 0–10 numerical rating scale; and could speak, read, and write in English. Exclusion criteria included self-reported serious problems with hearing, eyesight, or memory; diagnosed with any type of arthritis other than OA; treated for cancer in the last 3 years; had a steroid injection or knee replacement in the past 3 months; planned to have a knee replacement in the next 6 months; self-reported inability to complete the study procedures (i.e., telephone calls and program activities that involve reading and writing); lacked a reliable telephone number; and answered ≥2 items incorrectly on a 6-item screening for cognitive impairment.[29]

Study variables

Outcome

Current use of the following oral pharmacologic treatments for knee OA was assessed at baseline: acetaminophen, NSAIDs, COX-2 inhibitors, and opioid medications. Treatment use was assessed based on self-report with dichotomous variables indicating use or not of each of the OA medication of interest. The question was asked: “Do you currently use any of the following medications for joint pain or arthritis?” For this study, patients were grouped into three categories of analgesic use: oral opioids (with or without other oral analgesic treatments), oral non-opioid analgesics, and no oral analgesic use.

Exposure variables

Social support was assessed using a 4-item abbreviated version of the Medical Outcomes Study social support scale that represents four dimensions of social support: emotional/informational, tangible, affectionate, and positive social interaction.[30] The sum of responses to all items constitute the overall social support score. Score range is from 0 to 16, with a higher score indicating more social support.

Health literacy was assessed by the question, “How confident are you filling out medical forms by yourself?” This is the best single question to detect patients with inadequate or marginal health literacy.[31] The responses were dichotomized to those with adequate (“extremely”, “quite a bit”) and inadequate (“somewhat”, “a little bit”, “not at all”) health literacy. Level of depression was assessed using the Patient Health Questionnaire (PHQ-8), which assesses the Diagnostic and Statistical Manual of Mental Disorders-IV criteria for the diagnosis of depressive disorders.[32] PHQ-8 scores (range: 0–24) were used to differentiate between those with none-minimal (0–4), mild (5–9), moderate (10–14) and severe (≥15) depressive symptoms.[32]

Covariates

Demographic characteristics that were obtained included: age, sex, race, education (≤high school/general education equivalency diploma, some college or 2-year degree, ≥ 4-year college degree), annual income (<$20,000, $20,000–39,999, ≥$40,000), and current marital status (married/living with partner or not).

Clinical data that were collected included self-rated health (excellent, good, fair, poor) and body mass index (BMI). OA-related disease severity was assessed using the Western Ontario McMaster Universities Osteoarthritis Index (WOMAC).[33] Comorbid medical conditions were assessed using an interviewer-administered version of the Charlson Comorbidity Index.[34] BMI was assessed via chart review, and all else were assessed via patient-reported surveys.

Statistical analysis

Descriptive statistics, including means and standard deviations (SD) for continuous variables and frequencies and percentages for categorical variables, were calculated. Demographic, clinical, social health, and psychological health variables were compared by type of oral OA analgesic group using analysis of variance (ANOVA) tests for continuous variables and Pearson's χ^2 tests for categorical variables.

``Multinomial logistic regression models were used to estimate the unadjusted and adjusted relative risk ratios (RRRs) of using oral opioid or non-opioid analgesic (vs. no oral analgesic treatment), comparing patients by levels of social support, health literacy, and depressive symptoms. Relative risk was obtained by exponentiating the linear equations derived from each model, yielding regression coefficients that are RRRs for a unit change in each exposure variable of interest.[35] Separate models were used to estimate the unadjusted and adjusted RRRs of using oral opioid vs non-opioid analgesic, also comparing patients by the different exposure variables. Models were adjusted for age, sex, race, income, WOMAC, comorbidity, and BMI. Only variables that were previously associated with the outcome[5–11] and exposure variables and that do not lay in the causal pathway were considered as covariates. Self-rated health and marital status were also considered as covariates but were removed from the models due to high correlation (|correlation coefficient| ≥ 0.33) with other variables (comorbidity index and social support scores, respectively). All covariates were tested for collinearity using the same methodology. Fully adjusted models included all covariates and all exposure variables.

Results

Among 5,111 who were mailed an invitation to participate in the study and 67 who responded to the study brochures, 839 were screened for study eligibility (Supplement 1). While 351 did not meet the study inclusion criteria, 488 were found to be eligible. Among the eligible participants, 128 could not be further contacted or chose not to participate in the study. Their demographic characteristics and mean pain level were not significantly different from those who entered the study (data not shown).

A total of 360 veterans with symptomatic knee OA were included in the study (Table I). Mean age was 64.2 years, and 23.6% were women. By study design, 50% identified as non-Hispanic white and 50% identified as African-American. The majority had an annual income of <$40,000 (59.9%) and were not married/living with a partner (54.3%). Most (60.6%) reported having good or better health, and mean calculated BMI was 31.8. Mean WOMAC total score was 48.0.

Nearly a third (30.6%) reported using an oral opioid analgesic, with or without other oral analgesic medications. The majority of patients (54.2%) reported currently using a non-opioid oral analgesic for knee OA, such as acetaminophen, a NSAID, and/or a COX-2 inhibitor (Table II). Only 15.3% of participants were not using any oral medication for knee OA.

Table I
Sociodemographic, clinical and psychosocial characteristics among oral opioid analgesic users vs oral non-opioid analgesic users vs those not using any oral analgesic medication

	All ($N = 360$)	Opioid users* ($N = 110$)	Non-opioid analgesic users only ($N = 195$)	Non-oral analgesic users ($N = 55$)	p-value†
Demographic					
Age, M (SD)	64.2 (8.8)	62.5 (8.1)	64.3 (8.8)	67.1 (9.2)	0.006
Female, N (%)	85 (23.6%)	29 (26.4%)	45 (23.1%)	11 (20.0%)	0.641
Race, N (%)					
African-American	180 (50.0%)	54 (49.1%)	96 (49.2%)	30 (54.5%)	0.765
White	180 (50.0%)	56 (50.9%)	99 (50.8%)	25 (45.5%)	
Education, N (%)					
High school/GED or less	109 (30.3%)	34 (30.9%)	59 (30.3%)	16 (29.1%)	0.841
Some college or 2 year degree	161 (44.7%)	50 (45.5%)	88 (45.1%)	23 (41.8%)	
4 year college degree or greater	90 (25.0%)	26 (23.6%)	48 (24.6%)	16 (29.1%)	
Income, N (%)					
<$20,000	103 (30.4%)	40 (37.4%)	51 (28.0%)	12 (24.0%)	0.383
$20,000–39,999	100 (29.5%)	26 (24.3%)	58 (31.9%)	16 (32.0%)	
$40,000+	136 (40.1%)	41 (38.3%)	73 (40.1%)	22 (44.0%)	
Marital status, N (%)					
Married/living with partner	164 (45.7%)	51 (46.4%)	90 (46.4%)	23 (41.8%)	0.823
Not married/living with partner	195 (54.3%)	59 (53.6%)	104 (53.6%)	32 (58.2%)	
Clinical					
Self-rated health, N (%)					
Good or better	218 (60.6%)	46 (41.8%)	132 (67.7%)	40 (72.7%)	<0.001
Fair or poor	142 (39.4%)	64 (58.2%)	63 (32.3%)	15 (27.3%)	
BMI, M (SD)	31.8 (6.5)	33.0 (7.1)	31.3 (6.2)	31.6 (6.4)	0.088
WOMAC Total, M (SD)	48.0 (16.9)	54.5 (15.3)	45.7 (15.9)	42.7 (19.6)	<0.001
Charlson comorbidity, N (%)					
0–1	104 (28.9%)	22 (20.0%)	70 (35.9%)	12 (21.8%)	0.017
2–3	121 (33.6%)	39 (35.5%)	60 (30.8%)	22 (40.0%)	
4+	135 (37.5%)	49 (44.5%)	65 (33.3%)	21 (38.2%)	
Social & Psychological					
Social support, M (SD)	10.6 (3.9)	10.0 (3.9)	10.5 (3.8)	11.9 (3.9)	0.017
Confidence filling out medical forms (health literacy item), *n* (%)					
Adequate health literacy	284 (78.9)	83 (75.5)	153 (78.5)	48 (87.3)	0.210
Inadequate health literacy	76 (21.1)	27 (24.5)	42 (21.5)	7 (12.7)	
Depressive symptoms (PHQ-8), *n* (%)					
None	140 (38.9%)	28 (25.5%)	87 (44.6%)	25 (45.5%)	<0.001
Mild	118 (32.8%)	35 (31.8%)	61 (31.3%)	22 (40.0%)	
Moderate to severe	102 (28.3%)	47 (42.7%)	47 (24.1%)	8 (14.5%)	

Abbreviations: BMI, Body mass index; GED, General Educational Development; PHQ, Patient Health Questionnaire; WOMAC, Western Ontario & McMaster Universities Osteoarthritis Index.
* With or without other oral treatments.
† Chi-squared/Fisher's with categorical variables; ANOVA with continuous variables.

Demographic and clinical characteristics by OA treatment use

Patients using opioids, in comparison to those using non-opioid analgesics and those not using any oral analgesic, had a lower mean age (62.5 vs 64.3 vs 67.1, respectively, $P = 0.006$). Mean age by oral analgesic use group differed by only a few years, however. Opioid analgesic users, compared to the two other OA oral analgesic groups, were also much more likely to report having fair/poor instead of good/excellent health (58.2% vs 32.3% vs 27.3%, $P < 0.001$) and to have ≥4 comorbidity index scores (44.5% vs 33.3% vs 38.2%, $P = 0.028$). Opioid analgesic users also had significantly higher mean WOMAC total score compared to the other treatment groups (54.5 vs 45.7 vs 42.7, $P < 0.001$). No other demographic or clinical characteristics differed across OA treatment groups (Table I).

Social and psychological factors by OA treatment use

Mean social support score was lower among opioid analgesic users, compared to non-opioid medication and no oral medication users (10.0 vs 10.5 vs 11.9, $P = 0.017$); mean scores differed by just a few points, however. More than three quarters of participants had adequate health literacy. Adequate health literacy level was more often observed among non-oral analgesic users than others, but health literacy level did not significantly differ by OA treatment group (Table I). Having moderate to severe depressive symptoms was most common among opioid analgesic users (42.7% vs 24.1% among non-opioid analgesic users vs 14.5% among those not taking oral analgesics, $P < 0.001$); there was a three-fold difference in proportion between opioid and non-oral analgesic users and almost a two-fold difference in proportion between non-opioid and non-oral analgesic users.

Association of social/psychological health with OA treatment use

Table III shows the associations between the social and psychological health measures with oral analgesic use, unadjusted and adjusted for age, sex, race, income, WOMAC total score, comorbidity score, and BMI. Having a higher social support score was modestly but significantly associated with lower risk of non-opioid and opioid oral analgesic vs no oral analgesic use (unadjusted RRR 0.91, 95%CI 0.83–0.99, and 0.88, 95%CI 0.80–0.96, respectively). The effect estimate for the association between social support and lower risk of oral non-opioid vs no oral analgesic use was nearly identical but no longer statistically significant when adjusted for patient sociodemographic and clinical characteristics. The association between social support and lower risk of oral opioid vs no oral analgesic use was slightly reduced and remained statistically significant when adjusted for the same characteristics (adjusted RRR

Table II
Proportion of samples reporting use of oral analgesics for knee osteoarthritis

Treatment group	Treatment	N (%) sample reporting use of specific treatment	N (%) sample by treatment group
No oral analgesic	No oral analgesic	55 (15.3%)	55 (15.3%)
Oral non-opioid analgesic	Acetaminophen only	32 (8.9%)	195 (54.2%)
	Oral NSAIDs* only	111 (30.8%)	
	Acetaminophen and oral NSAIDs* only	52 (14.4%)	
Oral opioid analgesic	Opioids only	26 (7.2%)	110 (30.6%)
	Opioids with other oral analgesics	84 (23.3%)	

Abbreviations: NSAIDs, nonsteroidal anti-inflammatory drugs.
* Including cyclooxygenase-2 inhibitors.

0.90, 95%CI 0.82–1.00). In a fully adjusted model that included all covariates and other exposure variables, the RRRs for social support were further reduced and not significantly associated with oral opioid or non-opioid analgesic use. There was no statistically significant association between health literacy and type of oral analgesic use in the unadjusted or adjusted models (Table III). .

Having moderate-severe depressive symptoms was strongly associated with higher risk of oral opioid analgesic use compared to no oral analgesic and oral non-opioid analgesic use (unadjusted RRR 4.38, 95%CI 1.89–10.15 and 2.35, 95%CI 1.42–3.87, respectively). The effect estimate for the association between depression symptoms and oral opioid analgesic vs no oral analgesic use was reduced but remained statistically significant when adjusted for age, sex, race, income, WOMAC total score, comorbidity score, and BMI (adjusted RRR 3.24, 95% CI 1.20–8.73). This estimate was further reduced and remained statistically significant when additionally adjusted for health literacy and social support (fully adjusted RRR 2.96, 95%CI 1.08–8.07). The effect estimate for the association between depression symptoms and oral opioid vs oral non-opioid analgesic use was attenuated and was no longer statistically significant when adjusted for sociodemographic and clinical variables. In the fully adjusted model, the estimate minimally changed. The severity of depression symptoms was not statistically significantly associated with non-opioid oral medication use compared to no oral analgesic medication use in the unadjusted or adjusted models.

Discussion

In this cohort of patients with knee OA, we found that nearly a third of the patients used oral opioid analgesics to treat their knee OA symptoms. A majority of the patients used non-opioid oral analgesics. Our study showed that having moderate to severe depressive symptoms was independently associated with oral opioid analgesic use compared to no oral analgesic use among those with symptomatic knee OA. In addition, we found that opioid medication users reported the lowest level of social support. However, social support did not have a statistically significant association with oral analgesic use in OA management in our adjusted models. We also found that health literacy did not have a statistically significant association with OA treatment use.

Our study is the first to show an association between depression and oral opioid analgesic use among knee OA patients, independent of sociodemographic and clinical health factors. Previous cohort studies and population surveys suggest that patients with non-cancer pain with a coexisting mental health condition (e.g., mood or personality disorder) are more likely to receive opioids than those with similar pain level but without a mental health condition.[18–21] OA studies also reported that depression and anxiety contribute to increased hospitalization and utilization of healthcare providers.[16,36] In a study of women with physical disability, mostly due to OA, higher level of depression was associated with using a maximum dose of any analgesic medication.[37]

Why depression is linked to increased oral opioid medication use is unclear, but there are various potential explanations. Mental health conditions, such as depression, may lower the pain threshold and diminish responsiveness to opioids in patients with OA.[38,39] Individuals with mood disorder may be using opioids to “self-medicate” their emotional pain and its associated physical symptoms.[40] Those with mental health disease may be more likely to seek opioids for misuse than others.[18] Healthcare providers may also be more likely to prescribe opioids to those with mental health conditions who tend to have multiple clinical comorbidities.[20]

Table III
Social and psychological variables associated with oral analgesic use for knee osteoarthritis

	Unadjusted* relative risk ratio (95% CI)	*p*-value	Adjusted† relative risk ratio (95% CI)	*p*-value	Fully Adjusted‡ relative risk ratio (95% CI)	*p*-value
Social support						
Oral Non-Opioid Analgesic vs. No Oral Analgesic (Ref)	0.91 (0.83,0.99)	0.025	0.92 (0.84, 1.01)	0.085	0.94 (0.86,1.03)	0.188
Oral Opioid vs. No Oral Analgesic (Ref)	0.88 (0.80,0.96)	0.005	0.90 (0.82, 1.00)	0.044	0.92 (0.83,1.02)	0.120
Oral Opioid vs. Oral Non-Opioid Analgesic (Ref)	0.97 (0.91,1.03)	0.277	0.98 (0.92, 1.05)	0.519	0.98 (0.92,1.05)	0.601
Adequate health literacy §						
Oral Non-Opioid Analgesic vs. No Oral Analgesic (Ref)	0.53 (0.22,1.26)	0.151	0.46 (0.19, 1.13)	0.090	0.52 (0.21,1.30)	0.160
Oral Opioid vs. No Oral Analgesic (Ref)	0.45 (0.18,1.11)	0.082	0.45 (0.17, 1.18)	0.104	0.53 (0.20,1.42)	0.207
Oral Opioid vs. Oral Non-Opioid Analgesic (Ref)	0.84 (0.49,1.47)	0.547	0.97 (0.53, 1.79)	0.931	1.02 (0.55,1.89)	0.954
Depression, moderate to severe ‖						
Oral Non-Opioid Analgesic vs. No Oral Analgesic (Ref)	1.87 (0.82,4.23)	0.135	2.09 (0.80, 5.48)	0.133	1.93 (0.72,5.12)	0.189
Oral Opioid vs. No Oral Analgesic (Ref)	4.38 (1.89,10.15)	0.001	3.24 (1.20, 8.73)	0.020	2.96 (1.08,8.07)	0.035
Oral Opioid vs. Oral Non-Opioid Analgesic (Ref)	2.35 (1.42,3.87)	0.001	1.55 (0.88, 2.73)	0.131	1.53 (0.87,2.71)	0.140

Abbreviations: BMI, Body mass index; WOMAC, Western Ontario & McMaster Universities Osteoarthritis Index.
* Univariate multinomial model.
† Adjusted multinomial model adjusts for age, sex, race, income, WOMAC, comorbidity, and BMI.
‡ Final multivariate multinomial model includes social support, health literacy, depression level, age, sex, race, income, WOMAC, comorbidity, and BMI.
§ vs. inadequate health literacy.
‖ vs. mild-no depression.

In addition, there is substantial evidence that depressive symptoms are predictive of elevations in pain, including arthritis-related pain.[41,42] Depressive symptoms are also associated with greater odds of inadequate pain relief in knee OA.[43] While non-opioid analgesics are often the first-line medications used for the pharmacologic treatment of OA, depressive symptoms may reduce the response to initial pharmacologic treatments.[42,43] Consequently, those with more depressive symptoms are more likely to require second-line medications, including opioids. Conversely, those who are on opioids may be more likely to develop depressive symptoms than those who are not on opioids. It has been demonstrated in a large retrospective cohort study that opioid users have an up to two-fold increased risk of future depressive symptoms than opioid non-users.[44] Establishing a cause–effect relationship requires prospective studies.

Finding a significant association between depressive symptoms and opioid treatment use has important clinical implications. Educating healthcare providers about timely identification of mood disorders among those with OA may potentially minimize opioid dependence of patients living with this comorbidity. Implementation of screening questionnaires can help identify this psychological comorbidity at an early stage, which could lead to the early implementation of a management plan to improve the outcomes of patients with OA.[23] Implementing an anti-depressant therapy (e.g., duloxetine) in tandem with a NSAID or other non-opioid analgesics may also be appropriate.[1] As opioid use may also exacerbate depression,[44] OA patients who are prescribed opioids for pain must be followed very closely with ongoing assessment of benefits and risks, including the development or worsening of depressive symptoms. From a research standpoint, evaluating the effects of pharmacologic and non-pharmacologic treatments for depression on the utilization of opioid vs non-opioid analgesic use for OA would be an appropriate next step.

Our study adds to the literature by reporting no statistically significant association between health literacy and OA medication use. Evidence on the relationship between health literacy and healthcare service and rheumatologic treatment utilization is limited. Low health literacy often results in more frequent physician visits, non-physician clinic visits, and hospital admissions.[22,45] This suggests that those with limited health literacy, compared to those with adequate or high health literacy, may be more likely to receive a prescription for and use pharmacologic treatments, such as analgesic medications.

Our study results also showed that among those with knee OA, opioid medication users, in comparison to non-opioid medication users, had the lowest levels of social support. Among OA patients in Germany, living alone was the strongest factor associated with increased visits to a general practitioner.[16] Social support has distress-alleviating and stress-buffering effects.[46] Social support may act as a "buffer" to mitigate the severity of the disease, reducing the need for treatment. High social support has, in fact, been linked to decreased need of particular health services, such as nursing care and mental health service.[15,47] However, supportive social networks may also contribute to increase in general medical service use.[47] Being married, a structural measure of social support, has been associated with increased use of COX-2 inhibitors in a survey of community-dwelling adults with arthritis.[9] Our observed association between social support and oral OA treatment use was no longer statistically significant when adjusted for various demographic, clinical, and psychological factors. It is possible that these other factors, compared to social factors, may be more relevant determinants of OA oral analgesic treatment use.

Greater social support has been associated with higher physical functioning, general health, mental health, and vitality among those with OA.[48] Social support is also known to moderate the effects of pain, functional limitation, and depression in older adults with OA.[49] Interventions that promote social support by improving the quality of social relationships, especially those that strengthen ties with confidants, should be developed.[25] The effects of such interventions to the utilization of opioid vs non-opioid analgesic treatment for OA should also be tested.

Consistent with previous OA studies,[5–9,11] we found that opioid medication users had worse self-rated health, more clinical comorbidities, and more OA-related symptoms that opioid non-users. Increased number of co-morbidities has been positively associated with use of or prescription receipt for oral COX-2 selective NSAIDs and opioid agents for lower extremity OA.[7–9] Greater OA disease severity has also been associated with more oral prescription analgesic use for OA.[5–7,11] While greater OA disease severity may predict increased use of opioid medications, it is also possible the opioid use may worsen OA symptoms. Many of these OA studies[5–9] have a cross-sectional study design, and longitudinal studies are necessary to clarify this relationship.

We also found that opioid medication users were the youngest in our cohort. Consistent with the literature, younger age is often associated with use of any oral analgesic, NSAIDs and opioid medications among OA patients.[5–7] Sex, race, and income did not vary across OA oral treatment groups in our cohort. In contrast, female sex has been previously, but inconsistently, associated with increased use of any oral analgesic for OA,[5–11] and White OA patients are prescribed COX-2 selective NSAIDs and opioid analgesics[5,8] more often than their African-American counterparts. Low income is usually associated with current use of opioids but with decreased use of NSAIDs.[6,9] Inconsistencies between our findings and these other studies may be related to the fact that we examined clinical trial participants. Patients who participate in clinical trials often have different risk profiles compared with the broader population. Lack of association between a demographic characteristic and OA oral treatment use may be due to variations in the patient populations being studied.

There are several limitations to consider in interpreting our findings. First, we conducted a cross-sectional analysis of baseline data. Therefore, causal relationships cannot be ascertained. We cannot ascertain if depression causes an increase in oral opioid medication use, if opioid medication use leads to more symptoms of depression, or if treatment-resistant OA leads to either or both depression and use of opioids. Second, oral medication use was self-reported, which is susceptible to recall bias. However, questionnaires which measure medication use behaviors generally exhibit high concordance with non self-report methods.[50] In addition, medication use was assessed by a dichotomous variable, and does not provide more detailed information, such as the frequency and quantity of medication use. Third, we recruited research participants from a single state, and the generalizability of our study findings among knee OA patients living in other regions is unclear. Fourth, while we screened out those who were treated for cancer in the last 3 years, we did not inquire about any recent surgical procedure or other medical conditions that might have necessitated oral analgesic treatment use. Some may have reported oral analgesic treatment use for indications other than joint pain even though our treatment use question specifically asked for use of a medication for joint pain or arthritis.

Conclusions

Our study is the first to examine the association between psychological and social health factors and the use of different types of oral analgesics for knee OA. While nearly a third of the patients used oral opioid analgesics, the majority used only non-opioid oral analgesics to treat their knee OA symptoms. Our results showed

that opioid analgesic users, compared to others, were more like to have moderate to severe depressive symptoms and lower social support. Higher level of depression was independently associated with opioid analgesic use vs no oral analgesic use. Although further investigation using longitudinal data is needed, these cross-sectional findings underscore the need to pay attention to mental health issues in the management of patients with symptomatic knee OA.

Declarations

Contributors

ERV, LRMH and CKK were responsible for the study concept and design. LRMH, SI, AY and DSO acquired and analyzed the data. All authors interpreted the data. ERV was responsible for creating the first draft of the manuscript. All authors critically revised the manuscript for important intellectual content. CKK and LRMH were responsible for study supervision. All authors read and approved the final version of the manuscript.

Conflict of interest

None of the authors declare any potential conflicts of interest in regard to this manuscript. Potential conflicts outside of this work: CKK has received grants from Abbvie and EMD Serono and consulted for Astellas, EMD Serono, Thusane, Express Scripts and Novartis.

Funding

This work was supported by the Veterans Health Administration Health Services Research and Development Service (IIR13-080; Principal Investigator: Dr. Hausmann). Dr. Vina was supported in part by a K23 Career Development Award from the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS, K23AR067226). Dr. Ibrahim was supported in part by a K24 Mid-Career Development Award from the NIAMS (K24AR055259). The views expressed here are those of the authors and do not represent those of the National Institute of Arthritis and Musculoskeletal and Skin Diseases, the National Institutes of Health, or the United States Government.

Acknowledgements

The authors would like to thank all Staying Positive With Arthritis study staff and participants.

Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.joca.2019.01.010.

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