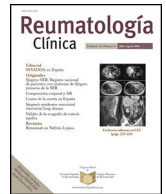




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## Original Article

# Results from a cross-sectional, observational study to assess inadequate pain relief in patients with knee and/or hip osteoarthritis in Mexico



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## ABSTRACT

**Introduction and objectives:** There is limited data that characterizes osteoarthritis (OA) patients who experience moderate to severe pain despite analgesic treatment in Mexico. In this study, we estimate the real-world prevalence of inadequate pain relief (IPR) among individuals with knee and/or hip OA who have been prescribed analgesic therapy and characterize this patient population for each country separately.

**Materials and methods:** This is a multinational, multi-site, cross-sectional, observational study. Participating physicians enrolled patients over 50 years of age with diagnosed knee and/or hip OA who had been prescribed topical and/or oral pain medication for at least 30 days prior to study visit, extracted data from their medical charts, and collected patient data using established questionnaires.

**Results:** 301 patients treated by 35 physicians in Mexico were enrolled in the study. More than half of the patients (53%) met the definition of IPR. Patients with IPR were significantly older (66.8 vs. 63.5 years,  $p=0.002$ ) and were more likely to be obese (24.2% vs. 11.9%,  $p=0.006$ ). Patients in the IPR group were more likely to report moderate/severe problems across all 5 dimensions of the EQ-5D and reported higher scores, indicating worse outcomes, on all three WOMAC subscales. Patients in the IPR group also reported reduced work productivity and greater treatment dissatisfaction compared to patients without IPR.

**Discussion and conclusions:** IPR is highly prevalent among individuals with knee and/or hip OA in Mexico. Patients with IPR experience decreased health-related quality of life HRQoL and work productivity, impaired function, and poor treatment satisfaction. Health care professionals need to be aware of the high prevalence of IPR, work toward improving OA patient management, and facilitate early intervention or changes in drug and other treatment modalities.

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## Resultados de un estudio transversal y observacional para valorar el alivio inadecuado del dolor en pacientes de osteoartritis de rodilla y/o cadera en México

## RESUMEN

**Introducción y objetivos:** Existen datos limitados que caractericen a los pacientes de osteoartritis (OA) que experimentan dolor de moderado a severo a pesar del tratamiento analgésico en México. En este estudio calculamos la prevalencia en el mundo real del alivio inadecuado del dolor (AID) entre individuos con OA de rodilla y/o cadera a quienes se ha prescrito terapia analgésica, y caracterizamos a esta población de pacientes por país, de manera separada.

### Palabras clave:

Osteoartritis  
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**Materiales y métodos:** Este estudio es multinacional, multicéntrico, transversal y observacional. Los médicos participantes reclutaron a pacientes mayores de 50 años, con diagnóstico de OA de rodilla y/o cadera, a quienes se había prescrito medicación analgésica tópica y/u oral durante al menos 30 días previos a la visita del estudio. Dichos facultativos extrajeron datos de sus cuadros médicos y recopilaron los datos de los pacientes utilizando cuestionarios establecidos.

**Resultados:** Se incluyó en el estudio a 301 pacientes tratados por 35 facultativos en México. Más de la mitad de los pacientes (53%) cumplió la definición de AID. Los pacientes con AID eran significativamente mayores (66,8 vs. 63,5 años,  $p = 0,002$ ) y con mayor probabilidad de ser obesos (24,2% vs. 11,9%,  $p = 0,006$ ). Los pacientes del grupo AID tenían mayor probabilidad de reportar problemas moderados/severos en las 5 dimensiones de EQ-5D, y reportaron puntuaciones más altas, lo cual es indicativo de peores resultados, en las tres subescalas de WOMAC. Los pacientes del grupo AID reportaron también una reducción de la productividad laboral y mayor insatisfacción con el tratamiento, en comparación con los pacientes sin AID.

**Discusión y conclusiones:** El AID es altamente prevalente entre los individuos con OA de rodilla y/o cadera en México. Los pacientes con AID experimentan una disminución de la calidad de vida relacionada con la salud (HRQoL) y la productividad laboral, deterioro funcional y mala satisfacción con el tratamiento. Los profesionales sanitarios deben ser conscientes de la alta prevalencia de AID, colaborar en la mejora del tratamiento de los pacientes de OA y facilitar la intervención temprana o los cambios de las modalidades de tratamiento farmacológico o de otro tipo.

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## Introduction

Osteoarthritis (OA) is a chronic musculoskeletal disorder characterized by the degeneration of cartilage and joints.<sup>1,2</sup> Commonly reported risk factors for the development of OA include age, gender, and biomechanical factors such as joint loading due to obesity or misalignment.<sup>3,4</sup> Pain is the most prominent and disabling symptom of OA patients. Pain is especially pronounced in patients with hip and knee OA as these are large weight-bearing joints.<sup>5–7</sup> In Latin America, the knee is the most frequently impacted joint in OA patients (31.2%–51.1%). OA of the hip occurs less frequently and is estimated to impact 1.3% of OA patients.<sup>3,8</sup>

Globally, OA is estimated to impact 4.2% of the population.<sup>9</sup> The burden of OA is projected to increase significantly in the future due to a combination of factors inclusive of an aging population, migration, and urbanization.<sup>9</sup> In Mexico, OA represents the most common rheumatic disease with prevalence estimates as high as 32% depending on the clinical definition of OA and the population in which prevalence is assessed.<sup>6,8–11</sup> Higher prevalence rates have been reported in specific geographies, older patient populations, and in women.<sup>6</sup> For example, the prevalence and impact of musculoskeletal and rheumatic diseases are particularly pronounced among the indigenous people of Latin America, inclusive of Mexico, due primarily to the physically demanding lifestyles in this population. A cross-sectional, community-based census study reported an OA prevalence as high as 32.2% in selected indigenous subpopulations.<sup>11</sup>

The Global Burden of Disease Study reports that musculoskeletal disorders, inclusive of OA, were ranked as one of the top ten contributors to disability in Mexico in 2016.<sup>9,12</sup> In Latin America, patients with symptomatic OA have been found to experience prolonged pain episodes, functional limitations, and worse general health status.<sup>11,13–15</sup> These studies highlight the high impact nature of OA and underscore the need for additional attention to patient treatment and management across several patient populations.

Clinical practice guidelines are primarily focused on the management of pain and recommend a range of pharmacologic therapies, such as paracetamol, nonsteroidal anti-inflammatory drugs (NSAIDs), and opioids, in addition to non-pharmacologic disease management approaches.<sup>16–18</sup> Despite the availability of multiple treatment options, effective pain management is not achieved for many OA patients. There are a number of challenges with successful management of pain in individuals with OA, which

include delayed diagnosis and treatment, limited treatment duration, unpredictable outcomes and effectiveness, patient-directed alterations in treatment regimens based on symptom severity, side effects, and increasing popularity in traditional medicines despite potential limitations.<sup>13,19</sup> Additionally, clinical guidelines may be unclear and challenging for treating physicians to implement in daily practice and social inequalities may limit access to appropriate care.<sup>16,20,21</sup>

There is limited data that characterizes patients who experience moderate to severe pain despite analgesic treatment in Mexico. A cross-sectional, observational study completed in Latin America evaluated patients with symptomatic knee OA. This study reported that even among the 71% of patients that had taken medications, pain was persistent, suggesting the presence of an ongoing unmet need in this patient population.<sup>13</sup> In Mexico, 28.5% of OA patients experienced pain improvement with medications and 7.1% with rest and medications.<sup>13</sup> A multinational European study also quantified the burden of inadequate pain relief (IPR), estimating an IPR prevalence of 54% of knee OA patients and demonstrating significant associations between IPR and worse health-related quality of life (HRQoL) or increased functional limitation.<sup>22</sup> The European survey of osteoarthritis real world therapies (SORT) study focused on western European countries (United Kingdom, France, Germany, Portugal, Italy, and the Netherlands), and thus are not generalizable to other regions of the world.<sup>22</sup>

In this study, which has been completed in the Philippines, Thailand, Russia, Mexico, and China, we aim to estimate the real-world prevalence of IPR among individuals with knee and/or hip OA who have been prescribed analgesic therapy, characterize this patient population for each country, and assess the impact of IPR on patient reported outcomes (PRO) inclusive of HRQoL, utilities, function, work productivity, and activity impairment. The results from the Mexico cohort are presented in this paper.

## Methods

### Study design

This was a multinational, multi-center, cross-sectional, non-interventional study designed to collect data via both retrospective medical chart review and patient reported outcomes (PROs) using instruments administered at a single study visit. This study was considered to be “research without risk” under the Mexican Gen-

eral Health Law, due to the retrospective, non-interventional study design. Eligible patients were consented prior to study participation. All patient data were de-identified and reported in aggregate.

#### Data collection

A sample of OA-treating physicians of various specialties (e.g., primary care, family practice, general practice, internal medicine, orthopedic surgery, rheumatology) were recruited for the study. A clinical expert was consulted to ensure the study included an adequate mix of physician specialties treating OA in Mexico. The participating physicians were responsible for the recruitment of knee and hip OA patients, the administration of PRO instruments at the site using paper questionnaires, and the extraction of clinical data from patient medical charts.

#### Inclusion/exclusion criteria

Patients were eligible for inclusion in the study if they were older than 50 years of age, had a diagnosis of OA in one or both knees and/or hip, and were prescribed topical and/or oral analgesics including paracetamol, NSAIDs, opioid, or combination therapy with traditional medicine, joint injections, or other regimens for at least 30 days prior to enrollment. Patients were not eligible for the study if they had a diagnosis of arthritis other than primary OA, had partial or total joint replacement, were treated with disease-modifying antirheumatic drugs, were scheduled to participate in a randomized control trial within 3 months of enrollment, or were diagnosed with comorbidities that significantly affected their pain ratings, work productivity, or activity impairment (e.g., cancer), or were unable/unwilling to adhere to study protocol requirements.

#### Study variables

##### Patient characteristics

Patient characteristics were captured using a pre-specified Case Report Form and included patient demographic (e.g., gender, age, weight/height, ethnicity, marital status, family history, living/care arrangements, smoking/employment status, insurance coverage) and clinical information (e.g., joints affected, diagnosis/follow up date, comorbidities, treatment received).

##### Brief pain inventory (BPI)

The BPI is a self-administered questionnaire to assess pain intensity and its effect on functional status. The pain severity is ranked on an 11-point scale over several time periods.<sup>23</sup> For this study, IPR was assessed using a score >4 on item 5: (“Please rate your pain by circling the one number that best describes your pain on the average”).<sup>22</sup>

##### Euro-QoL five dimensions (EQ-5D)

The EQ-5D can be used to assess general health status. The instrument itself collects data on 5-health dimensions (Mobility, Self-Care, Usual Activities, Pain/Discomfort, Anxiety/Depression). The patient rates perceived problems based on a 5-level severity scale (level 1 denoting “no problems” to level 5 denoting “severe/extreme problems”). The health state utility score (EQ-5D Index) is derived from the descriptive system. The score ranges from 0 to 1; where 0 indicates patient experience akin to death and 1 indicating perfect health. A higher score suggests greater utilities associated with the current health state.<sup>24–27</sup> The Spanish version of the EQ-5D instrument for Mexico was administered to the patient population, however, there currently is no valuation set for Mexico, thus the authors used the most recent valuation sets published for the Latin American region. The EQ-5D Index was calculated using the EQ-5D-5L value set developed for a Uruguay

population.<sup>28</sup> Finally, the EQ-5D Visual Analog Scale (VAS) was used to record the patients’ self-rated health on a scale with endpoints labeled “the best health you can imagine = 100” and “the worst health you can imagine = 0”.<sup>24–27</sup>

##### Work productivity/activity impairment (WPAI)

The WPAI questionnaire measures the impact of disease on a patient’s employment status and activity. It is comprised of six questions designed to assess employment status, missed work hours due to the disease and the extent to which the disease interfered with work productivity (from “no effect on my work” to “completely prevented me from working”) in the last seven days. WPAI also measures the extent to which the disease limited a patient’s daily activities unrelated to work. Based on responses to these questions, absenteeism, presenteeism, and overall work impairment were calculated.<sup>29</sup>

##### Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC)

The WOMAC scale is used to assess function of daily living (17 items), stiffness (2 items), and pain (5 items). The response items are on 10-point scales, and the score for each dimension was the sum of scores for each item. Therefore, the possible score ranges are 0–170 for daily living, 0–20 for stiffness, and 0–50 for pain, with a higher score indicating worse function.<sup>30</sup>

##### Patient global assessment/patient satisfaction with OA treatments

Patients were asked to rate the impact of disease status on their daily lives (“Considering all the ways your problems with your joints affect you, mark an (X) in one box below for how well you are doing”). The response was recorded using five categories ranging from “very well” to “poor”. In addition, a question was asked to assess the patients’ treatment satisfaction. The response was recorded using the seven categories ranging from “extremely dissatisfied” to “very satisfied”.

##### Statistical analysis

##### IPR prevalence

The prevalence of IPR was estimated based on patients reporting a score greater than 4 on BPI Question 5 (“Please rate your pain by circling the one number that best describes your pain on the average”).<sup>22</sup>

##### Patient characteristics and IPR

Patients with or without IPR were compared using descriptive statistics. Patients demographic/clinical characteristics and PROs were summarized for each cohort using continuous (mean, standard deviation [SD], median, minimum/maximum) or categorical measures (frequency and percent). Continuous variables were compared using the Wilcoxon Rank Sum test, and the categorical variables were compared using Chi-Square or Exact Fisher test. A multivariate logistic regression was performed to identify predictors of IPR.

##### IPR and patient reported outcomes

Generalized linear models (GLM) were used to evaluate the relationship between IPR and patient outcomes, while controlling for relevant covariates. For EQ-5D Visual Analog Scale (VAS) and EQ-5D Index, GLM with gamma distribution and beta regression was used, respectively. Other PRO variables were predicted using GLM with negative binomial distribution. All statistical tests were interpreted using 2-tailed significance levels.

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**Table 1**  
Participating physicians characteristics.

Variable	Category	Physicians (N = 35)
Gender of physician, N (%)	Male	23 (65.7%)
Age of physician, N (%)	30–39	21 (60.0%)
	40–49	8 (22.9%)
	50–59	3 (8.6%)
	60–69	3 (8.6%)
Practice setting, N (%)	Hospital-based	12 (34.3%)
	Private practice/office-based	8 (22.9%)
	Both	15 (42.9%)
Primary medical specialty, N (%)	Rheumatologist	15 (42.9%)
	Orthopedist/Orthopedic surgeon	11 (31.4%)
	Primary care physician (FP/GP)	3 (8.6%)
	Internal medicine specialist	6 (17.1%)
Academic/teaching responsibilities, N (%)	Yes	26 (74.3%)
Total patients with primary OA of the knee or hip manage/treat per month	Mean (SD)	77.60 (104.22)

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## Results

A geographically dispersed sample of 35 physicians actively treating patients with OA of the knee and/or hip were included in the study. During study recruitment, 377 total physicians were screened and contacted for participation and 62 responded to participate. The characteristics of the participating physicians ( $N=35$ ) are provided in Table 1. The physicians were mostly male (65.7%) and between the ages of 30–49 (82.9%). Most physicians were either rheumatologists (42.9%) or orthopedist/orthopedic surgeons (31.4%), and 74% had teaching responsibilities.

The patient baseline characteristics are presented in Table 2. The mean age of all patients ( $N=301$ ) included in the study was  $65.2 \pm 9.6$  years. There was a predominance of females in our study sample (73.4%). Most patients in the study had knee OA (70.8%), and 59% of patients had reports of OA in more than one joint.

All patients in the study received analgesic therapy for at least 30 days prior to study enrollment. On average patients received 2 different classes of pain medications. The most commonly prescribed treatment was NSAIDs (84.4%), followed by paracetamol (33.2%), chondroprotective compounds (16.6%), and opioids (15.6%).

About half of the patients were categorized as having IPR ( $N=158$ ; 52.5%). Patients with IPR were significantly older than patients without IPR (66.8 vs. 62.5 years;  $p=0.002$ ). The mean body mass index (BMI) was  $28.6 \text{ kg/m}^2$  for all patients, however those with IPR had significantly higher BMI compared to patients without IPR ( $29.2 \text{ kg/m}^2$  vs.  $28.0 \text{ kg/m}^2$ ;  $p=0.040$ ) and a significantly higher proportion of IPR patients were categorized as obese (24% vs. 12%;  $p=0.006$ ).

The predictors of IPR identified from a logistic regression model included physician primary specialty and academic responsibilities, and patient characteristics including age, BMI, depression, diabetes, and hyperlipidemia (all  $p<0.05$ ). Specifically, patients older than 70 years of age had 2.5 times higher chance of having IPR than those younger than 60 years old ( $p=0.013$ ). Obese patients were also 2.5 times more likely to have IPR compared to patients with normal BMI ( $p=0.036$ ).

Patients with IPR reported more problems with each of the five dimensions of the EQ-5D. For example, moderate to severe problems with mobility was reported in 71.5% of patients with IPR and 37.1% of patients without IPR ( $p<0.001$ ). Additionally, patients reporting the presence of IPR were more likely to report that they were either severely or extremely anxious or depressed (0.7% vs.

20.3%). Table 3 summarizes the patient-reported problems with each of the dimensions of the EQ-5D.

Overall, patients with IPR reported less treatment satisfaction compared to patients without IPR (25% vs. 67%,  $p<0.001$ ). The adjusted means for PRO outcomes from multivariable analysis are summarized in Table 4. Overall, patients with IPR reported worse scores across all PROs. Results were statistically significant ( $p<0.05$ ) for all comparisons except absenteeism, presenteeism, and work productivity, which were assessed using the WPAI. Compared to patients without IPR, patients with IPR reported lower EQ-5D VAS score (75.5 vs. 61.3,  $p<0.001$ ) and EQ-5D Index (0.771 vs. 0.656,  $p<0.001$ ). WOMAC scores were higher among patients with IPR in all three subdomains (all  $p<0.001$ ). WPAI activity impairment score was higher in patients with IPR (52.1 vs. 29.3,  $p<0.001$ ).

## Discussion

To our knowledge, this is the first study to evaluate the real-world occurrence and impact of IPR in OA patients in Mexico. This study demonstrates an association between IPR in OA patients receiving analgesics and HRQoL, function, work productivity, and daily activities. The results of the IPR-specific analyses were consistent with previous study reports on IPR in knee OA patients published for a European population.<sup>22</sup>

Our findings regarding the impact of pain, as the primary symptom of OA, are also consistent with studies assessing the overall impact and burden associated with OA.<sup>13–15</sup> In a cross-sectional, community study of 439 OA patients, Esquivel-Valerio et al., assessed the impact of OA in a low-income urban population in Mexico.<sup>15</sup> The authors showed that patients with OA had a poorer perception of their health compared to the general population and reported greater disability (Health Assessment Questionnaire – Disability Index [HAQ-DI]), more functional limitations, and greater pain and discomfort.<sup>15</sup> Similarly, a hospital based cross-sectional study completed in Mexico examined disease activity scores (DAS28), the HAQ-DI, and WOMAC among other measures to quantify the impact of OA in comparison with other chronic diseases. In this study, Ambriz Murillo et al., concluded that patients with OA and other rheumatic diseases experienced more pain than patients with other chronic conditions (i.e., end-stage renal disease, diabetes).<sup>14</sup>

Possible explanations for persistent IPR may include lack of non-pharmacologic interventions (e.g., weight control), poor treatment effectiveness, decline in effectiveness over time, poor patient management, presence of comorbidities, or barriers to treatment access/health care system characteristics. An analysis of

**Table 2**  
Patient demographic and clinical characteristics.

Variable	Statistic or category	All (N = 301)	Without IPR (N = 143)	With IPR (N = 158)	p-Value
Age (years)	Mean (SD)	65.22 (9.62)	63.48 (9.48)	66.80 (9.51)	0.002
	50–60	114 (37.9%)	66 (46.2%)	48 (30.4%)	0.006
	61–70	99 (32.9%)	46 (32.2%)	53 (33.5%)	
	>70	88 (29.2%)	31 (21.7%)	57 (36.1%)	
Gender, N (%)	Female	221 (73.4%)	104 (72.7%)	117 (74.1%)	0.795
Body Mass Index (kg/m <sup>2</sup> )	Mean (SD)	28.63 (4.53)	27.96 (4.59)	29.17 (4.43)	0.040
	Underweight	2 (0.7%)	1 (0.7%)	1 (0.6%)	0.068
	Normal	48 (15.9%)	27 (18.9%)	21 (13.3%)	
	Overweight	101 (33.6%)	46 (32.2%)	55 (34.8%)	
	Obese	88 (29.2%)	33 (23.1%)	55 (34.8%)	
Unknown	62 (20.6%)	36 (25.2%)	26 (16.5%)		
Other comorbidities (OARSI-related) <sup>a</sup> , N (%)	Yes	183 (60.8%)	81 (56.6%)	102 (64.6%)	0.160
Duration of OA diagnosis (years)	Mean (SD)	3.73 (4.16)	3.38 (3.06)	4.05 (4.94)	0.508
Number of joints affected, N (%)	1	123 (40.9%)	58 (40.6%)	65 (41.1%)	0.817
	2	96 (31.9%)	48 (33.6%)	48 (30.4%)	
	3	32 (10.6%)	16 (11.2%)	16 (10.1%)	
	4+	50 (16.6%)	21 (14.7%)	29 (18.4%)	
Joints affected, N (%)	Hip-only	47 (15.6%)	20 (14.0%)	27 (17.1%)	0.729
	Knee-only	213 (70.8%)	104 (72.7%)	109 (69.0%)	
	Both	41 (13.6%)	19 (13.3%)	22 (13.9%)	
Treatment, N (%)	NSAIDs	254 (84.4%)	120 (83.9%)	134 (84.8%)	0.831
	Opioid-based	47 (15.6%)	12 (8.4%)	35 (22.2%)	0.001
	Chondroprotective	50 (16.6%)	28 (19.6%)	22 (13.9%)	0.188
	Antispasmodic	3 (1.0%)	2 (1.4%)	1 (0.6%)	0.606
	Steroid	8 (2.7%)	2 (1.4%)	6 (3.8%)	0.287
	Viscosupplement	10 (3.3%)	4 (2.8%)	6 (3.8%)	0.753
	Paracetamol	136 (45.2%)	65 (45.5%)	71 (44.9%)	0.928
	Other Analgesic	1 (0.3%)	1 (0.7%)	0 (0.00%)	0.475
	Non-pharmacologic	100 (33.2%)	50 (35.0%)	50 (31.6%)	0.541
Number of different pain medication classes	Mean (SD)	2.12 (1.07)	2.06 (0.96)	2.17 (1.16)	0.753

<sup>a</sup> OARSI (Osteoarthritis Research Society International)-related comorbidities include: diabetes, hypertension, cardiovascular disease, renal failure/dysfunction, GI bleed, depression, obesity, physical impairment, and myocardial infarction.<sup>1</sup>

**Table 3**  
EQ-5D descriptive results for patients with and without IPR.

Dimension/level	All patients (N = 301) N (%)	Without IPR (N = 143) N (%)	With IPR (N = 158) N (%)	p-Value
<b>Mobility</b>				<0.001
I have no problems walking	35 (11.6%)	24 (16.8%)	11 (7.0%)	
I have slight problems walking	100 (33.2%)	66 (46.2%)	34 (21.5%)	
I have moderate problems walking	108 (35.9%)	49 (34.3%)	59 (37.3%)	
I have severe problems walking	50 (16.6%)	2 (1.4%)	48 (30.4%)	
I am unable to walk	8 (2.7%)	2 (1.4%)	6 (3.8%)	
<b>Self-care</b>				<0.001
I have no problems washing or dressing myself	112 (37.2%)	69 (48.3%)	43 (27.2%)	
I have slight problems washing or dressing myself	86 (28.6%)	43 (30.1%)	43 (27.2%)	
I have moderate problems washing or dressing myself	83 (27.6%)	29 (20.3%)	54 (34.2%)	
I have severe problems washing or dressing myself	17 (5.6%)	1 (0.7%)	16 (10.1%)	
I am unable to wash or dress myself	3 (1.0%)	1 (0.7%)	2 (1.3%)	
<b>Usual activities</b>				<0.001
I have no problems doing my usual activities	52 (17.3%)	38 (26.6%)	14 (8.9%)	
I have slight problems doing my usual activities	103 (34.2%)	62 (43.4%)	41 (25.9%)	
I have moderate problems doing my usual activities	105 (34.9%)	39 (27.3%)	66 (41.8%)	
I have severe problems doing my usual activities	37 (12.3%)	3 (2.1%)	34 (21.5%)	
I am unable to do my usual activities	4 (1.3%)	1 (0.7%)	3 (1.9%)	
<b>Pain/discomfort</b>				<0.001
I have no pain or discomfort	3 (1.0%)	3 (2.1%)	0 (0.00%)	
I have slight pain or discomfort	101 (33.6%)	70 (49.0%)	31 (19.6%)	
I have moderate pain or discomfort	121 (40.2%)	59 (41.3%)	62 (39.2%)	
I have severe pain or discomfort	65 (21.6%)	10 (7.0%)	55 (34.8%)	
I have extreme pain or discomfort	11 (3.7%)	1 (0.7%)	10 (6.3%)	
<b>Anxiety/depression</b>				<0.001
I am not anxious or depressed	132 (43.9%)	87 (60.8%)	45 (28.5%)	
I am slightly anxious or depressed	91 (30.2%)	36 (25.2%)	55 (34.8%)	
I am moderately anxious or depressed	45 (15.0%)	19 (13.3%)	26 (16.5%)	
I am severely anxious or depressed	28 (9.3%)	1 (0.7%)	27 (17.1%)	
I am extremely anxious or depressed	5 (1.7%)	0 (0.00%)	5 (3.2%)	



**Table 4**  
Multivariate models to assess impact of IPR on PRO outcomes.

Outcomes	Without IPR (N = 143)		With IPR (N = 158)		p-Value
	Mean	SE	Mean	SE	
EQ-5D VAS	75.49	1.64	61.37	1.55	<0.001
EQ-5D Index	0.771	0.015	0.656	0.017	<0.001
WOMAC pain subscale score	13.62	1.25	28.75	2.40	<0.001
WOMAC stiffness subscale score	5.31	0.51	10.46	0.90	<0.001
WOMAC physical function subscale score	48.31	4.38	97.25	8.00	<0.001
WPAI presenteeism	25.02	5.04	48.59	11.52	0.055
WPAI absenteeism	9.86	3.39	29.40	13.25	0.089
WPAI work productivity loss	30.50	6.44	56.91	14.19	0.071
WPAI activity impairment	29.27	2.70	52.14	4.33	<0.001

Model adjusted for: age, year since diagnosis/follow up, gender, body mass index, number of medication classes, insurance status, physician characteristics, joints affected, diabetes, cardiovascular disease, hyperlipidemia/hypertension, and depression.

data collected for an indigenous patient population in Latin America suggests that access to medical care is a particular challenge – 40.6% of this patient population reported having never sought medical or traditional treatment despite reports of pain, disability, and challenges with coping.<sup>11</sup> Further research is needed to understand system factors that may be contributing to the high prevalence of IPR and to help inform strategies for improved patient treatment and management.

As part of this study, we investigated the utilization of different pain medications in Mexico. Our finding that OA patients receive combination therapies or medications across multiple classes was consistent with larger population-based studies.<sup>3</sup> Additionally the study results were in agreement with previously published literature that the most commonly used pain medications in Mexico are NSAIDs.<sup>3</sup> An observational study of 3040 OA patients in Latin America reported that NSAIDs were used in 68.5% of the OA population in the region and 50.1% in Mexico. The same study reported higher utilization of vicosupplementation (27.5%) in Mexico compared to other countries compared to other countries in the region, which was an observation that was not replicated in our current study.<sup>3</sup> Additional studies from Mexico have reported NSAID utilization rates between 50 and 60%.<sup>8,13,20</sup>

There are limitations to the study which need to be acknowledged. First, the information in the chart could be incomplete, with patients receiving care from other physicians. Not all clinical outcomes that could influence physician-prescribing behavior or treatment decisions are necessarily measured and/or recorded in the chart. For example, patient compliance to prescribed treatment regimens was not assessed as part of this study. Moreover, there exists potential recall bias in PROs as they were provided by the patients. Second, there is a potential selection bias in patient selection, and the prevalence derived from the study is estimated from a convenient sample. Therefore, the estimates are not population-derived. Third, because of the cross-sectional nature of conducting the survey, causal relationship between IPR and PROs may not be established. The results should be interpreted with these limitations in mind.

## Conclusion

A large proportion of patients with OA in Mexico suffer from IPR (52.5% of the study population), which is associated with significant impairment in patient's quality of life and functional status.

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## Conflict of interest

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