

# A Secondary Analysis: Comparison of Experimental Pain and Psychological Impact in Individuals with Carpometacarpal and Knee Osteoarthritis

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**Purpose:** Evaluate sensory and psychological differences in individuals with thumb carpometacarpal (CMC) and/or knee osteoarthritis (OA) pain. This secondary analysis focuses on comparing the effects of OA at large and small joints in community-dwelling adults.

**Patients and Methods:** A total of 434 individuals were recruited from communities in Gainesville, FL and Birmingham, AL. Each participant completed health and clinical history questionnaires, quantitative sensory testing, and physical functional tests. Participants were divided into four groups based on their pain (“CMC pain” (n = 33), “knee pain” (n = 71), “CMC + knee pain” (n = 81), and “pain-free” controls (n = 60)). ANCOVAs were performed to identify significant differences in experimental pain and psychological variables across groups.

**Results:** The “CMC + knee pain” group had lower pressure pain thresholds (lateral knee site,  $p < 0.01$ ) and higher temporal summation of mechanical pain (knee,  $p < 0.01$ ) when compared to “CMC pain” and “pain-free” groups. The “knee pain” group had lower heat pain tolerance at the forearm site ( $p = 0.02$ ) and higher mechanical pain ( $p < 0.01$ ) at both tested sites in comparison to the “CMC pain” group. Lastly, the “CMC + knee pain” group had the highest self-reported pain ( $p < 0.01$ ) and disability ( $p < 0.01$ ) compared to all other groups.

**Conclusion:** Results suggest knee OA compounded with CMC OA increases disease impact and decreases emotional health compared to OA at either the CMC or knee joint alone. Results also support a relationship between the number of painful joints and enhanced widespread pain sensitivity. Measuring pain at sites other than the primary OA location is important and could contribute to more holistic treatment and prevention of OA progression.

**Keywords:** thumb, trapeziometacarpal, multi-site OA, generalized OA, quantitative sensory testing

## Introduction

Osteoarthritis (OA) is a multifactorial musculoskeletal and degenerative disease that can affect any joint.<sup>1</sup> Yet, most studies focus solely on large joints, namely the hip or knee. A systematic review that compared knee, hip, and hand OA found that the hand exhibits the highest radiographic prevalence of OA but is included in the lowest number of studies.<sup>2</sup> Moreover, studies typically focus on single-site OA, but OA can affect multiple joints within an individual. For example, it is common for individuals with knee OA to also suffer from hand OA.<sup>3,4</sup> The similarities and differences in factors contributing to the clinical presentation of OA at a single, large lower extremity joint; a single, small hand joint; or across multiple joints in the body are unknown, highlighting important knowledge gaps in our understanding of OA phenotypes.

An important aspect of the clinical presentation of OA at any joint is pain. The complexity of osteoarthritic pain is attributed to the combined influences of psychological factors,<sup>5</sup> disease pathophysiology,<sup>6</sup> and multiple aspects of

nociceptive processing, including changes in nociceptive receptors,<sup>7,8</sup> presence of neuropathic pain,<sup>9–11</sup> and altered pain modulation.<sup>12</sup> Notably, recent clinical and experimental studies have shown sensitization of pain pathways during OA, involving changes in joint nociceptors and central nervous system pain processing.<sup>13–15</sup> Most of these experimental studies have evaluated pain mechanisms through a combination of psychological assessments and quantitative sensory testing (QST). For example, studies of knee OA have used psychological assessments to inform targeted treatments<sup>16–18</sup> and QST to identify clinically meaningful characteristics.<sup>19,20</sup>

In comparison, although the body of work on hand OA is growing, investigation of somatosensory disparities and phenotypes in individuals with hand OA remains limited.<sup>21–26</sup> The few studies that measured pain phenotypes at the hand showed that participants with symptomatic hand OA demonstrated higher self-reported hand pain as well as peripheral<sup>26</sup> and central<sup>15</sup> sensitization in comparison to healthy or control participants. Similarly, few studies have evaluated alterations in nociceptive processing and/or pain phenotypes in symptomatic, multi-joint OA.<sup>27–29</sup> This limited literature means that to our knowledge, no studies focused on hand OA or multi-joint OA with hand involvement include a complete sensory assessment (eg, mechanical and thermal); instead, most studies focus solely on pressure stimulus,<sup>25,30</sup> or report clinical or psychological characteristics without QST measures.<sup>31</sup> Examining measures of self-reported pain, psychological, and somatosensory function simultaneously may allow more general conclusions regarding altered pain processing in these populations. Further study could also elucidate to what extent results from research examining large joint OA generalize to the small non-load-bearing joints of the hand and/or multi-joint OA.

As a step toward understanding the impact of small, large, and multi-joint involvement on the multidimensional pain experience, this study aimed to evaluate sensory and psychological differences in individuals with carpometacarpal (CMC) OA and/or knee OA compared to “pain-free” controls. CMC OA was chosen as a representative form of small joint OA because it occurs in isolation more frequently than OA at other joints in the hand.<sup>32</sup> Knee OA was chosen as a representative form of large joint OA due to its wide study and the fact that it is known to occur concomitantly with hand OA.<sup>33</sup> In this secondary analysis of previous studies focused on osteoarthritic disease,<sup>34,35</sup> we specifically examined differences in somatosensory (ie, QST) and psychological function across four groups of individuals (ie, only “CMC pain”, only “knee pain”, “CMC + knee pain”, and “pain-free” controls). Given the population demographics, physical examination, and reported symptoms, OA was the most likely cause of pain in the pain groups. We hypothesized that the “CMC + knee pain” group would have significantly higher experimental pain and worse functional impact than the only CMC, only knee, and “pain-free” groups.

## Materials and Methods

### Study Design

The primary objective of the study was to elucidate differences in pain and psychological limitations in individuals with only “CMC pain”, individuals with only “knee pain”, “CMC + knee pain”, and “pain-free” individuals. This study is a secondary data analysis from community-dwelling individuals that participated in the Understanding Pain and Limitations in OsteoArthritic Disease-1 (UPLOAD1) and Understanding Pain and Limitations in OsteoArthritic Disease-2 (UPLOAD2) studies at the University of Florida (UF) and the University of Alabama Birmingham (UAB). Each of these studies featured distinct cohorts, comprising individuals with knee OA as well as a corresponding control group. These cohorts were merged and analyzed together for the purposes of this study given similarities in inclusion/exclusion criteria, recruitment methods, and study procedures.<sup>17,36</sup> Briefly, participants in both studies provided informed consent and completed a series of questionnaires that assessed demographics, functional factors, and psychosocial characteristics. In addition, participants attended a quantitative sensory session (QST) undergoing thermal, mechanical, and temporal summation of pain assessments. Institutional Review Boards at the UF and UAB approved both studies (IRB# 201400209, IRB# 201500906), and a preliminary version of this secondary analysis was published as a conference abstract.<sup>37</sup>

### Participants

Both UPLOAD1 and UPLOAD2, included individuals between 45 and 85 years of age, who self-identified as non-Hispanic Black/African American or non-Hispanic White/Caucasian or European. Posteroanterior and lateral radiographs of the

knee were taken to clinically diagnose participants with bilateral or unilateral knee OA.<sup>38</sup> Participants were excluded if they had any of the following: 1) clinically significant surgery to the affected (ie, most painful) knee including total joint replacement; 2) systematic rheumatic disorders including rheumatoid arthritis, lupus erythematosus, and fibromyalgia; 3) peripheral neuropathy; 4) psychiatric illness requiring hospitalization within the previous year; 5) cognitive impairment; 6) daily opioid use; 7) uncontrolled hypertension, heart failure, or history of acute myocardial infarction. All participants underwent a physical exam by a clinician, including assessment of pain evoked by manual palpation of carpal and metacarpal joints bilaterally. Given this physical exam and the strict exclusion of rheumatic disorders, the most likely explanation for reported CMC pain is OA; however, presence of CMC OA was not confirmed via radiograph.

## Description Quantitative Sensory Testing Procedure

### Mechanical

Pressure pain thresholds were evaluated at the medial and lateral aspects of the affected knee, ipsilateral quadriceps, and trapezius using a calibrated algometer (AlgoMed, Medoc). The order of testing sites was randomized for all participants. For each site, a handheld algometer was applied at a constant rate of 30 kPa/second until the participant indicated the sensation “first became painful.” An average pressure pain threshold of three trials was determined for each site. As a safety measure, the maximum pressure that can be applied for the knee sites was 600 kPa and 1000 kPa at the other sites.<sup>39</sup>

### Thermal

Thermal stimuli were applied to the affected knee (or a randomly selected knee for “pain-free” individuals) and ipsilateral ventral forearm using a computer-controlled Medoc PATHWAY Pain & Sensory Evaluation System. Heat pain thresholds and tolerances were assessed using a 16×16 mm thermode. The baseline temperature started at 32°C and increased at a rate of 0.5°C/second. For the heat pain threshold, temperature was recorded when participant stated the sensation “first became painful”. Similarly, the temperature was recorded for heat pain tolerance when the participant was no longer able to tolerate the pain.

### Temporal Summation (TS)

TS of heat pain was evaluated at the dorsal forearm and the affected knee or randomly selected knee for “pain-free” individuals. Participants were asked to rate the intensity of peak pain during a series of 5 brief and repetitive heat pulses (CHEPS, Medoc). During the trials, 3 different temperatures were used (44°C, 46°C, and 48°C). The difference between the fifth trial and first trial pain rating was used as an indicator of temporal summation of heat pain.

TS of punctate pain was evaluated using a calibrated Von Frey monofilament with a target force of 300 grams. This test was performed at the affected patella or right patella for “pain-free” individuals and back of the left hand in randomized order. Using the pain scale of 0 to 100, participants reported their pain rating after a single contact and after 10 consecutive contacts. The difference between the pain rating after 10 contacts and the pain rating after a single contact was used as an indicator of TS for each site.

## Pain Characteristics

Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) was used to assess symptoms of knee OA in the past 48 hours.<sup>40</sup> The WOMAC has 3 categories, including pain during activities (5 items), stiffness during the day (2 items), and impairments in physical function (17 items), with higher scores indicating worse outcomes.

Graded Chronic Pain Scale (GCPS) was used to analyze global pain severity and pain-related interference over the past 6 months. Participants were asked to complete a series of 7 items related to pain intensity and pain interference using a 0–10 numeric rating scale. Scores were averaged and multiplied by 10 to generate a GCPS characteristic pain intensity score and GCPS disability score, with higher scores indicating greater pain.

Number of Pain Sites was collected from all participants. They were asked to self-report body site where they experienced pain on most days over the past 3 months. The sum of all areas reported represents the total number of pain sites.

## Psychological and Physical Function

Coping Strategies Questionnaire-Revised (CSQ-R) was used to evaluate passive and active coping techniques related to pain.<sup>41</sup> Using a 7-point scale, participants rated the frequency with which they engage in various coping techniques (ie, ignoring, praying, catastrophizing). A higher score indicating a greater use of that coping strategy.

Life Orientation Test- Revised (LOT-R) was used to measure how optimistic or pessimistic people feel about the future through a 10-item scale.<sup>42</sup> Optimism has been shown to improve physical and mental health and work performance,<sup>43</sup> with higher scores indicating more optimism.

Positive and Negative Affect Schedule (PANAS) was used to characterize different feeling and emotions through a set of 20 words associated with positive and negative affect.<sup>44</sup> Participants were asked to choose how they generally feel that way on a 1–5-point scale from very slightly to extremely. Higher scores on positive affect demonstrate positive feelings (eg, enthusiasm, energy), while high scores on negative affect demonstrate negative feelings (eg, distress).

Short Physical Performance Battery (SPPB) was used to assess physical function. This battery is a reliable and valid performance-based measure of physical function commonly used for patients with knee OA.<sup>34</sup> It evaluates standing balance, 4-meter gait speed, and chair rising tasks. Scores ranging from 0 to 12 are calculated, with lower scores indicating greater functional limitations.

## Statistical Methods

Individuals were categorized into four groups based on the baseline questionnaires and health history assessment (Table 1). In addition to indicating no joint pain during their physical examination, the “pain-free” group only included individuals that also scored 0 on the WOMAC-pain and GCPS questionnaires. Definition of these groups enabled testing of our hypothesis that individuals with multi-site OA (“CMC + knee pain” group) would have significantly higher experimental pain and worse psychological impact in comparison to single-site OA (“CMC pain” only and “knee pain” only groups) and “pain-free” individuals.

Data analysis was performed using IBM SPSS software v.28. Values convey the mean ± standard deviation (SD), unless stated otherwise. Demographic characteristics were examined using chi-square for nominal variables and t-tests for continuous/discrete ordinal variables. To assess differences across the four groups, analysis of covariance (ANCOVA) was conducted. Effect sizes are reported as partial eta squared ( $\eta^2$ ) where  $\eta^2 = 0.01$  indicates a small effect,  $\eta^2 = 0.06$  indicates a medium effect, and  $\eta^2 = 0.14$  indicates a large effect. Fisher's Least Significant Difference (LSD) post hoc tests were performed to compare group means. Location of primary pain differences in QST and psychological measures was examined in a model with no covariates (ie, unadjusted model) and a second model with sex, education, and income as covariates given previous literature<sup>45–47</sup> (ie, fully adjusted model). The unadjusted model serves as a baseline, while the adjusted model accounts for significant differences in demographics between groups. Statistical significance was set at *p* values less than or equal to 0.05.

**Table 1** Joint Pain Indicated During Physical Examination

GROUPS	CMC Joint Pain		Other Hand Pain		Knee Pain	
	Right	Left	Right	Left	Right	Left
“CMC Pain” (n=33)	✓	✓	✓	✓	X	X
“Knee Pain” (n=71)	X	X	X	X	✓	✓
“CMC + knee Pain” (n=81)	✓	✓	✓	✓	✓	✓
“Pain-free” (n=60)	X	X	X	X	X	X

**Notes:** “✓” denotes inclusion of participants with listed pain per group, while “X” denotes exclusion. Inclusion in all pain groups did not mandate bilateral pain; individuals with either right or left-side pain were also considered. The “CMC Pain” and “Pain-free” groups were identified from the control group in the original study. If the “CMC Pain” group excluded individuals with other hand pain only *n* = 15 participants would be eligible. Similarly, the “CMC + knee pain” group also included individuals with hip pain. If hip pain were excluded only *n* = 30 participants would be eligible.

## Results

### Demographic and Descriptive Statistics

Two hundred and forty-five of 434 subjects met the eligibility criteria of having either CMC, knee, or CMC and knee pain in this secondary analysis. Significant sex, education, and annual income differences were shown across groups ( $p < 0.05$ ) (Table 2). There were no significant differences in age or race across groups.

### Pain Group Differences in Experimental Pain Measures

The “CMC + knee pain” had significantly lower pressure pain thresholds at the lateral knee site and mechanical TS at the knee in comparison to the only “CMC pain” group and “pain-free” group in the fully adjusted model (all  $p$ 's  $< 0.01$ ) (Table 3). For the unadjusted model, the “CMC + knee pain group” had significantly lower pressure pain threshold at all body sites with exception of the trapezius (all  $p$ 's  $< 0.01$ ), and lower heat pain tolerance (forearm,  $p < 0.01$ ; knee,  $p = 0.02$ ) when compared to the only “CMC pain” and “pain-free” groups. The “CMC + knee pain” group also had higher heat induced TS at the forearm (at 46 °C,  $p < 0.01$ ) in comparison to all other pain groups (Figure 1).

When comparing the only “CMC pain” and “knee pain” groups, the “knee pain” individuals had significantly lower pressure pain threshold at the knee sites (medial,  $p = 0.03$  and lateral,  $p < 0.01$ ) and higher mechanical TS pain at both sites ( $p$ 's  $< 0.01$ ) in the fully adjusted model. Differences between only “CMC pain” and only “knee pain” were also observed in the unadjusted model during the heat pain tolerance, mechanical TS, and pressure pain threshold at all sites with exception of the quadriceps. No significant differences were observed for heat pain thresholds across groups in either model.

### Pain Group Differences in Psychological Variables

The “CMC + knee pain” group had the highest self-reported pain, disability, and emotional distress compared to all other groups (Figure 2). Specifically, the “CMC + knee pain” group had significantly higher pain intensity, disability, and stiffness per the GCPS and WOMAC questionnaires and lower outcomes during the SPPB ( $p < 0.01$ ) in comparison to the only “CMC pain” group in the fully adjusted model (all  $p$ 's  $< 0.01$ ) (Table 4). Similarly, the “CMC + knee pain” group was also significantly different from the only “knee pain” group in the disability portion of the GCPS questionnaire and SPPB outcomes. We also observed significant differences in number of pain sites between the only “knee pain” group and “CMC + knee pain” group, but no significant differences were observed across only “knee pain” and “CMC

**Table 2** Subject Demographics by Location of Primary Pain Groups

	<b>CMC Pain (n=33)</b>	<b>Knee Pain (n=71)</b>	<b>CMC + Knee Pain (n=81)</b>	<b>Pain-Free (n=60)</b>	<b>P-value</b>
<b>Age, mean <math>\pm</math> SD</b>	59.85 $\pm$ 7.19	55.89 $\pm$ 6.98	58.37 $\pm$ 7.64	57.35 $\pm$ 8.86	0.070
<b>Race, % (Count)</b>					0.290
African American	48.5 (16)	52.1 (37)	46.9 (38)	35.6 (21)	
Non-Hispanic white	51.5 (17)	47.8 (34)	53.1 (43)	64.4 (38)	
Other				1.7 (1)	
<b>Sex, % (Count)</b>					<b>0.010</b>
Female	75.8 (25)	62.0 (44)	80.2 (65)	56.7 (34)	
Male	24.2 (8)	38.0 (27)	19.8 (16)	43.3 (26)	
<b>Education (Count)</b>					<b>0.002</b>
$\leq$ High school	24.2 (8)	50.7 (36)	56.8 (46)	30.0 (18)	
Some College	45.5 (15)	36.6 (26)	35.8 (29)	50.0 (30)	
$\geq$ College Degree	30.3 (10)	12.7 (9)	7.4 (6)	20.0 (12)	
<b>Annual Income</b>					<b>0.007</b>
<\$40,000	39.4 (13)	67.1 (47)	74.7 (59)	48.3 (29)	
\$40,000 – \$80,000	27.3 (9)	21.4 (15)	16.5 (13)	35.0 (21)	
>\$80,000	33.3 (11)	11.4 (8)	8.9 (7)	16.7 (10)	

**Note:** Bolded text shows statistical significance.

**Table 3** Results of Quantitative Sensory Testing by Location of Primary Pain Groups (Mean ± SD) and Comparison Across Groups

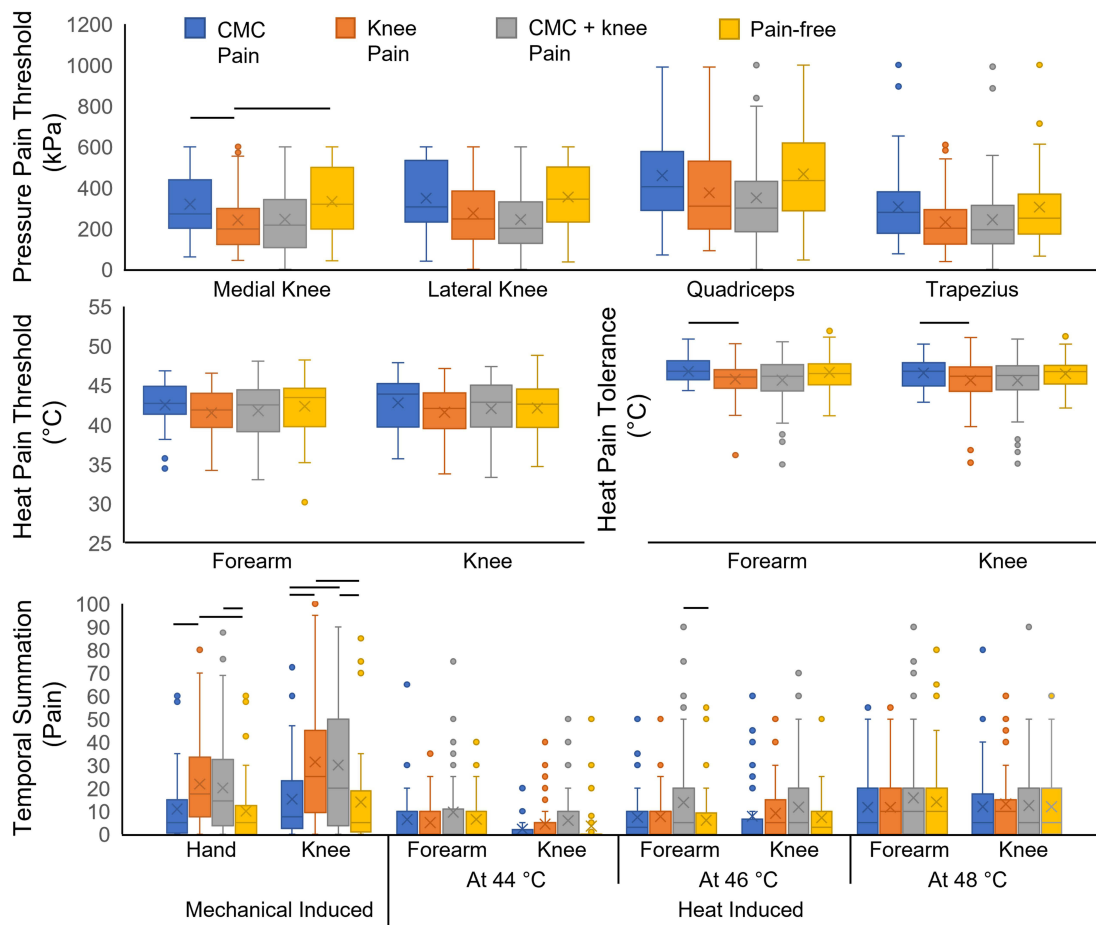
	CMC Pain (n=33)	Knee Pain (n=71)	CMC + Knee Pain (n=81)	Pain-Free (n=60)	Unadjusted		Fully Adjusted	
					η <sup>2</sup>	P-value	η <sup>2</sup>	P-value
<b>Pressure Pain Threshold, kPa</b>								
Knee								
Medial	318.7 ± 156.7	240.9 ± 156.1	250.7 ± 153.4	328.1 ± 167.3	0.060	<b>0.002</b> <sup>a,b,e,f</sup>	0.038	<b>0.030</b> <sup>a,e</sup>
Lateral	347.9 ± 168.3	279.2 ± 159.5	247.3 ± 153.6	349.6 ± 162.1	0.075	<b>&lt;0.001</b> <sup>a,b,e,f</sup>	0.049	<b>0.008</b> <sup>a,b,e,f</sup>
Quadriceps	459.1 ± 234.8	375.0 ± 209.4	353.9 ± 207.3	457.5 ± 235.9	0.048	<b>0.008</b> <sup>b,e,f</sup>	0.022	0.151
Trapezius	306.6 ± 212.1	231.3 ± 136.7	246.2 ± 180.5	301.9 ± 191.5	0.034	<b>0.042</b> <sup>a,e</sup>	0.023	0.139
<b>Heat Pain Threshold, °C</b>								
Knee								
Forearm	42.8 ± 3.5	41.6 ± 3.1	42.1 ± 3.5	42.2 ± 3.3	0.012	0.387	0.013	0.377
Forearm	42.5 ± 3.1	41.5 ± 3.0	41.8 ± 3.5	42.3 ± 3.5	0.013	0.351	0.009	0.554
<b>Heat Pain Tolerance, °C</b>								
Knee								
Forearm	46.7 ± 1.8	45.4 ± 2.5	45.5 ± 3.2	46.4 ± 1.8	0.039	<b>0.022</b> <sup>a,b,e</sup>	0.020	0.185
Forearm	46.8 ± 1.6	45.5 ± 2.1	45.6 ± 3.0	46.6 ± 2.1	0.046	<b>0.009</b> <sup>a,b,e,f</sup>	0.020	0.197
<b>TS – Heat Induced Pain</b>								
At 44 °C								
Forearm	7.1 ± 13.0	5.3 ± 8.0	10.6 ± 15.9	6.6 ± 10.3	0.031	0.065	0.023	0.159
Knee	2.6 ± 5.4	4.9 ± 8.8	6.2 ± 11.3	3.5 ± 9.2	0.019	0.223	0.006	0.713
At 46 °C								
Forearm	7.8 ± 11.9	8.4 ± 8.6	14.5 ± 20.4	6.2 ± 11.2	0.054	<b>0.006</b> <sup>b,c,f</sup>	0.028	0.096
Knee	8.9 ± 15.9	11.4 ± 17.3	12.4 ± 16.6	7.1 ± 10.7	0.018	0.243	0.007	0.686
At 48 °C								
Forearm	12.5 ± 15.9	13.4 ± 13.9	17.1 ± 20.3	14.2 ± 18.7	0.010	0.531	0.004	0.834
Knee	13.6 ± 19.1	15.1 ± 16.6	13.5 ± 16.7	11.9 ± 14.9	0.004	0.819	0.005	0.778
<b>TS – Mechanical Pain</b>								
Knee								
Hand	15.3 ± 18.6	31.4 ± 27.5	30.4 ± 29.9	14.1 ± 21.4	0.088	<b>&lt;0.001</b> <sup>a,b,e,f</sup>	0.061	<b>0.002</b> <sup>a,b,e,f</sup>
Hand	10.0 ± 14.5	21.8 ± 18.3	20.4 ± 20.1	10.9 ± 15.6	0.081	<b>&lt;0.001</b> <sup>a,b,e,f</sup>	0.064	<b>0.001</b> <sup>a,b,e,f</sup>

**Notes:** Bolded text shows statistical significance. Some individual data points are missing for some subjects. With exception of heat temporal summation which has a maximum of 8 missing subjects in the “CMC + knee Pain” group, all other modalities never have more than 2 missing subjects. <sup>a</sup>Is significant differences between “CMC Pain” and “Knee Pain”. <sup>b</sup>Is significant differences between “CMC Pain” and “CMC + knee Pain”. <sup>c</sup>Is significant differences between “Knee Pain” and “CMC + knee Pain”. <sup>d</sup>Is significant differences between “Knee Pain” and “Pain-free”. <sup>e</sup>Is significant differences between “CMC + knee Pain” and “Pain-free”.

pain” or “CMC pain” and “CMC + knee pain” in the fully adjusted model. When comparing coping strategies, the “CMC + knee pain” group used reinterpretation more commonly than the only “CMC pain” and “knee pain” groups. Interestingly, the sole distinction in coping strategies between the “CMC pain” and “knee pain” groups, within the fully adjusted model, emerged during praying, where the “knee pain” group demonstrated higher scores. Although no comparisons were made within-groups for the coping strategies, the raw values show that the only ‘CMC pain’ and ‘CMC + knee pain’ groups had higher scores for coping self-statements, while the only ‘knee pain’ group chose praying as a coping mechanism more often.

## Discussion

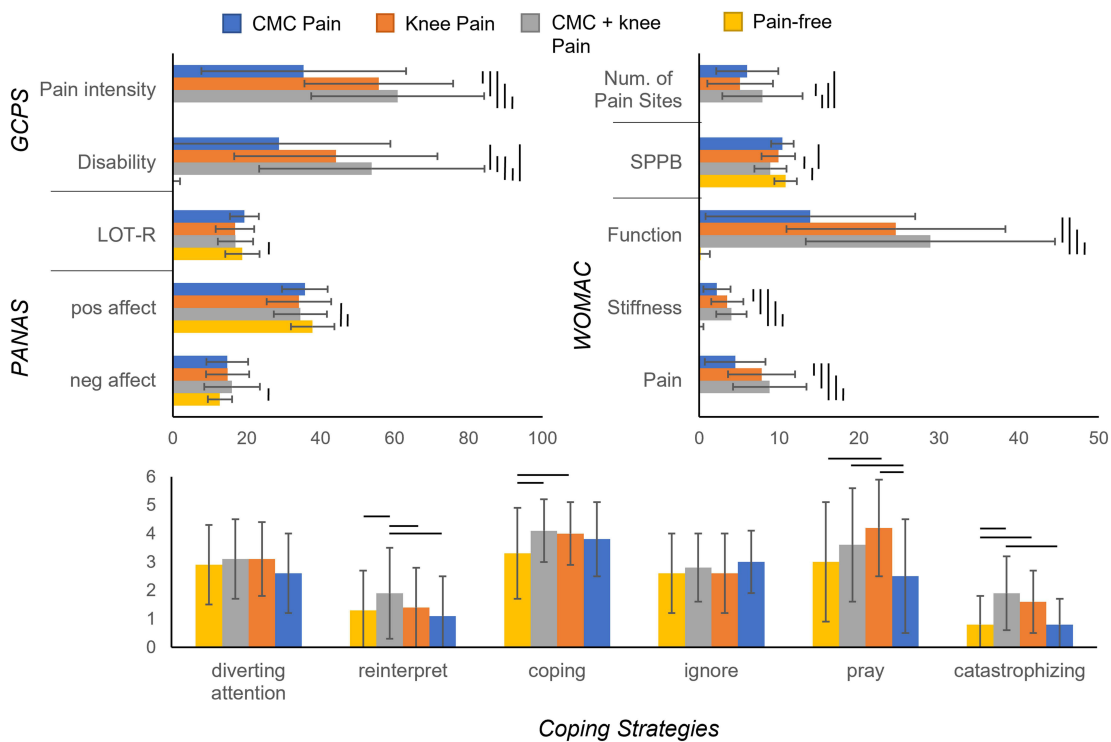
The primary finding of this secondary analysis is that individuals with “CMC + knee pain” had higher functional disability and greater psychological symptoms than individuals with “CMC pain” or “knee pain”. Both pain intensity and the overall self-perceived disability were significantly higher, or more severe, when knee OA was compounded with “CMC pain”. This finding is in agreement with previous studies that showed pain severity and the feeling of helplessness directly affect self-perceived disability<sup>48,49</sup> as well as studies that have shown that individuals with multi-joint pain have worse self-reported function and physical performance than those with single-joint pain.<sup>28</sup>



**Figure 1** Results of quantitative sensory testing by location of primary pain groups. Boxplots represent the distribution of the data, where “x” represents the mean, “—” represents the median, and dots represent outliers. Black lines represent statistically significant differences between cohorts.

To our knowledge, even though hand OA is commonly diagnosed in conjunction with knee OA,<sup>29,50</sup> this is the first study to explicitly compare pain and psychological factors in “CMC pain” and “knee pain” groups. When comparing pain groups, we found significant differences in pressure pain threshold, heat pain tolerance, and mechanical temporal summation. Our results showed that the only “CMC pain” group experienced less pain during mechanical TS and had higher pressure pain threshold at the knee sites when compared to the only “knee pain” group in the fully adjusted model. However, in contrast to previous studies reporting that individuals with CMC OA experience pressure pain hyperalgesia<sup>25</sup> in comparison to a healthy cohort, our study identified no differences between the “CMC pain” and “pain-free” groups. Remarkably, the “CMC + knee pain” group had the highest pain ratings during TS at the forearm at all temperatures in comparison to all other groups, but was only significantly different in the unadjusted model at 46 °C. These results suggest that individuals with knee pain exacerbated with CMC pain may experience hyperalgesia in the arm more frequently than individual with either just “CMC pain” or “knee pain”.

This study also provides novel insights into the psychological symptoms and functional disability experienced by individuals with hand and/or knee OA. Functional limitation scores during the SPPB of the “CMC + knee pain” group were significantly lower than those in the “CMC pain” and “knee pain” group in the fully adjusted model. These results can be related to their pain scores during the assessment, unfortunately due to missing data this type of analysis was not completed. Furthermore, coping mechanisms used in response to disability varied across groups. The “CMC + knee pain” and “CMC pain” groups demonstrated a preference for using coping statements, while the “knee pain” group dealt with the pain by praying. Interestingly, the second most common coping mechanism chosen by the “CMC pain” group, which



**Figure 2** Results of function and psychological variables by location of primary pain groups. Error bars represent standard deviations. Black lines represent statistically significant differences between cohorts.

also had the highest raw scores in comparison to all other groups, was ignoring. Given that the thumb accounts for over 50% of hand function,<sup>51</sup> these results imply individuals with “CMC pain” are ignoring pain during a wide variety of activities of daily living, thereby highlighting the need for future work to identify effective treatments for CMC pain, so that pain is eliminated and coping is no longer necessary.

This study was a secondary analysis of existing datasets collected to understand pain characteristics in patients with knee OA. As such, there are several limitations. Because the focus of the original study was characterizing knee pain, most of the QST assessments did not include the CMC joint or the hand as a testing site. Despite this limitation, the results highlighted differences in clinical and experimental pain across individuals with only “CMC pain”, only “knee pain”, and “CMC + knee pain”. Additionally, significant differences in self-perceived pain intensity and functional limitations were identified across groups. For example, although psychological questionnaires for hand OA were not assessed (eg, AUSCAN or DASH), the higher scores in the WOMAC of the “CMC + knee pain” group and only “knee pain” group highlights the severity of disability in individuals with multi-site OA, particularly OA compounded with CMC joint pain. Another limitation was the absence of medical images confirming the presence of OA. However, given the demographics of the population and exclusion criteria (eg, presence of rheumatoid OA, fibromyalgia, lupus) and the physical examination performed, it is likely that pain in the hand was the result of OA. The self-reported number of pain sites and the fact that only “CMC pain” and “knee pain” groups included individuals with bilateral joint pain might be reflective of the participants age<sup>52</sup> and may render our findings more representative of the broader community. Moreover, our groups were created based on their most painful joint and excluding as necessary pain at the hand or knee joints. Lastly, the study includes groups with different numbers of individuals. However, due to the large overall number of individuals studied, our analyses were powered to detect group differences that are moderate in magnitude.

**Table 4** Results of Function and Psychological Variables by Location of Primary Pain Groups (Mean  $\pm$  SD) and Comparison Results

	CMC Pain (n=33)	Knee Pain (n=71)	CMC + Knee Pain (n=81)	Pain-free (n=60)	Unadjusted		Fully Adjusted	
					$\eta^2$	P-value	$\eta^2$	P-value
<b>GCPS</b>								
Pain intensity	35.4 $\pm$ 27.7	55.7 $\pm$ 20.1	60.8 $\pm$ 23.4	0.0 $\pm$ 0.0	0.607	<b>&lt;0.001</b> <sup>a,b,d,e,f</sup>	0.589	<b>0.001</b> <sup>a,b,d,e,f</sup>
Disability	28.7 $\pm$ 30.1	44.1 $\pm$ 27.5	53.8 $\pm$ 30.5	0.2 $\pm$ 1.7	0.411	<b>&lt;0.001</b> <sup>a,b,c,d,e,f</sup>	0.366	<b>0.001</b> <sup>b,c,d,e,f</sup>
<b>WOMAC</b>								
Pain	4.5 $\pm$ 3.8	7.8 $\pm$ 4.2	8.8 $\pm$ 4.6	0.0 $\pm$ 0.0	0.476	<b>&lt;0.001</b> <sup>a,b,d,e,f</sup>	0.430	<b>0.001</b> <sup>a,b,d,e,f</sup>
Stiffness	2.2 $\pm$ 1.7	3.5 $\pm$ 2.0	4.0 $\pm$ 1.9	0.1 $\pm$ 0.4	0.461	<b>&lt;0.001</b> <sup>a,b,d,e,f</sup>	0.430	<b>0.001</b> <sup>a,b,d,e,f</sup>
Function	13.9 $\pm$ 13.1	24.6 $\pm$ 13.7	28.9 $\pm$ 15.6	0.2 $\pm$ 1.1	0.457	<b>&lt;0.001</b> <sup>a,b,c,d,e,f</sup>	0.405	<b>0.001</b> <sup>a,b,d,e,f</sup>
<b>SPPB</b> ,total score	10.4 $\pm$ 1.4	9.9 $\pm$ 2.1	8.9 $\pm$ 2.0	10.8 $\pm$ 1.4	0.132	<b>&lt;0.001</b> <sup>b,c,e,f</sup>	0.067	<b>0.001</b> <sup>b,c,f</sup>
<b>Number of Pain Sites</b>	6.0 $\pm$ 3.9	5.1 $\pm$ 4.1	7.9 $\pm$ 5.0	0.0 $\pm$ 0.0	0.377	<b>&lt;0.001</b> <sup>b,c,d,e,f</sup>	0.331	<b>0.001</b> <sup>c,d,e,f</sup>
<b>CSQ</b>								
Diverting-Attention	2.6 $\pm$ 1.4	3.1 $\pm$ 1.3	3.1 $\pm$ 1.4	2.9 $\pm$ 1.4	0.015	0.328	0.003	0.850
Reinterpret	1.1 $\pm$ 1.4	1.4 $\pm$ 1.4	1.9 $\pm$ 1.6	1.3 $\pm$ 1.4	0.044	<b>0.014</b> <sup>b,c,f</sup>	0.040	<b>0.024</b> <sup>b,c,f</sup>
Coping	3.8 $\pm$ 1.3	4.0 $\pm$ 1.1	4.1 $\pm$ 1.1	3.3 $\pm$ 1.6	0.061	<b>0.002</b> <sup>e,f</sup>	0.058	<b>0.003</b> <sup>e,f</sup>
Ignore	3.0 $\pm$ 1.1	2.6 $\pm$ 1.4	2.8 $\pm$ 1.2	2.6 $\pm$ 1.4	0.016	0.277	0.022	0.164
Pray	2.5 $\pm$ 2.0	4.2 $\pm$ 1.7	3.6 $\pm$ 2.0	3.0 $\pm$ 2.1	0.088	<b>&lt;0.001</b> <sup>a,b,e</sup>	0.063	<b>0.002</b> <sup>a,c,e</sup>
Catastrophizing	0.8 $\pm$ 0.9	1.6 $\pm$ 1.1	1.9 $\pm$ 1.3	0.8 $\pm$ 1.0	0.147	<b>&lt;0.001</b> <sup>a,b,e,f</sup>	0.083	<b>0.001</b> <sup>b,e,f</sup>
<b>LOT-R</b>	19.3 $\pm$ 3.9	16.8 $\pm$ 5.2	16.9 $\pm$ 4.8	18.8 $\pm$ 4.6	0.048	<b>0.010</b> <sup>a,b,e,f</sup>	0.026	0.114
<b>PANAS</b>								
Positive affect	35.7 $\pm$ 6.2	34.1 $\pm$ 8.7	34.5 $\pm$ 7.2	37.8 $\pm$ 5.9	0.046	<b>0.015</b> <sup>e,f</sup>	0.040	<b>0.030</b> <sup>e,f</sup>
Negative affect	14.7 $\pm$ 5.6	14.8 $\pm$ 5.8	16.0 $\pm$ 7.5	12.7 $\pm$ 3.3	0.042	<b>0.021</b> <sup>e,f</sup>	0.028	0.098

**Notes:** Bolded text shows statistical significance. Some individual data points are missing for some subjects. With the exception of the PANAS questionnaire which has a maximum of 7 missing subjects in the “CMC + knee Pain” group, all other variables never had more than 3 missing subjects. <sup>a</sup>Is significant differences between “CMC Pain” and “Knee Pain”. <sup>b</sup>Is significant differences between “CMC Pain” and “CMC + knee Pain”. <sup>c</sup>Is significant differences between “Knee Pain” and “CMC + knee Pain”. <sup>d</sup>Is significant differences between “CMC Pain” and “Pain-free”. <sup>e</sup>Is significant differences between “Knee Pain” and “Pain-free”. <sup>f</sup>Is significant differences between “CMC + knee Pain” and “Pain-free”.

## Conclusion

The differences in experimental pain and psychological variables found in this study highlight the importance of studying the pain experience across OA in both large and small joints. Given the “CMC + knee pain” group had the worst psychophysical outcomes, this highlights the importance of understanding CMC OA as a compounding factor for osteoarthritic pain at other joints. Given these findings, future studies should control how hand pain affects function and well-being. The results of this study also motivate future work to specifically study individuals with only CMC OA. Quantifying their experience thoroughly (eg, assessing pain thresholds at the CMC joint) could further our understanding of hand pain phenotypes and inform treatment.<sup>53</sup> Hand OA remains understudied despite its high prevalence.<sup>54</sup> Thus, expanding research of small joints is critical for fully elucidating their role in modulating the experimental and clinical pain experience.

## Abbreviations

CMC, carpometacarpal; OA, osteoarthritis; QST, quantitative sensory testing; TS, temporal summation; WOMAC, western Ontario and McMaster universities osteoarthritis index; GCPS, graded chronic pain scale; CSQ-R, coping strategies questionnaire-revised; LOT-R, life orientation test-revised; PANAS, positive and negative affect schedule; SPPB; short physical performance battery; SD, standard deviation.

## Ethics Approval of Research on Humans

The procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000.

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## Disclosure

The authors report no conflicts of interest in this work.

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