Positive affect and chronic pain: a preregistered systematic review and meta-analysis

Anthony D. Ong a,c,*, Felix Thoemmes a, Kaylin Ratner a, Kate Ghezzi-Kopel b, M. Carrington Reid c

Abstract
Chronic noncancer pain (CNCP) is a significant health burden among adults. Standard behavioral therapies typically focus on targeting negative affect (NA) and yield only modest treatment effects. The aims of this study were to systematically review and investigate the association between positive affect (PA) and pain severity among adults with CNCP. Databases that were searched included MEDLINE (PubMed), PsycINFO, CINAHL, ProQuest Dissertations and Theses, OLASTER, Open Grey, and PsyArXiv (inception to July 23, 2019). We analyzed studies that: (1) used observational, experimental, or intervention study designs; (2) enrolled individuals with CNCP (pain ≥ 12 weeks); and (3) reported full quantitative results on outcomes. Two researchers independently screened articles, extracted data, and assessed the risk of bias. The main meta-analysis was followed by subgroup analyses. All analyses were performed using random-effects models. Formal tests for heterogeneity (Q-statistic; I²) and publication bias (p-curve and p-uniform) were performed. We meta-analyzed 29 studies with 3521 participants. Results demonstrated that PA inversely impacts pain severity in people with CNCP (r = −0.23). Subgroup analyses showed a significant effect for gender and marginally significant effects for age in studies that adjusted for NA. On average, effect sizes for observational studies were larger in studies with a higher proportion of female respondents and in studies that did not adjust for NA. Finally, larger effect sizes were found in intervention studies with older compared with younger samples.

Keywords: Positive affect, Chronic pain, Pain severity, Systematic review, Meta-analysis

1. Introduction
It is estimated that 70 million Americans—more than the number affected by diabetes, heart disease, and cancer combined—suffer from chronic noncancer pain (hereafter referred to as CNCP) each year. With an increased prevalence among persons aged 65 years and older, chronic pain is a significant health burden—not just in terms of pain-related health care expenditures and disability, but also in terms of the inestimable costs to families and individual daily living and quality of life. Pain severity, a core clinical measure of chronic musculoskeletal pain, is associated with greater disability, sleep impairment, psychosocial difficulties, and increased prevalence of mental health disorders including depression, anxiety, and substance abuse among patients with CNCP. Although there is increasing interest in the use of evidence-based nonpharmacological approaches to managing chronic pain severity, standard behavioral therapies, such as cognitive-behavioral therapy (CBT) and mindfulness-based stress reduction (MBSR), typically focus on targeting negative affective states (eg, anxiety and depression) and yield only modest treatment effects. Efforts are therefore needed to develop more effective psychological treatments for chronic pain by identifying new targets for intervention.

A growing body of theory and research suggest that positive affective states (eg, gratitude and happiness) play a uniquely important role in promoting psychological adjustment in the face of chronic pain. Specifically, positive affect (PA) has been theorized to facilitate adaptive coping in the context of chronic pain by countering the negative effects of fear on attention; buffering negative pain-related cognitions (ie, rumination, helplessness, and magnification); reducing inflammation; promoting neutral reappraisal processes related to pain; and enhancing engagement in valued activities in the face of pain.

Although narrative reviews have been conducted to date, there has not been a comprehensive quantitative review relating PA to chronic pain severity. Howell et al. meta-analyzed experimental studies and found that induced PA was associated with higher pain tolerance. More recently, Kushlev et al. examined data from nearly 2.5 million U.S. respondents and found an inverse relationship between PA and previous-day physical pain. Notably, both studies focused on acute pain responses. Thus, there is a need to establish whether these findings generalize to chronic pain. The primary aim of this systematic review and meta-analysis was to comprehensively review the literature examining the association of PA and pain severity in people with CNCP. We use systematic methods and standardized procedures for locating and evaluating the relevance and quality of observational, experimental, and intervention studies. Observational studies consisted of both ambulatory and longitudinal studies. Ambulatory studies used experience sampling
methodology across several days or weeks to examine how changes in PA relate to pain. Longitudinal studies explored whether levels of PA predict future levels of pain across more extended periods. Experimental studies determined the effects of induced or manipulated PA on concurrent pain. Intervention studies examined the efficacy of PA-enhancing treatments on pain severity prospectively over time. The study’s secondary aims were to investigate moderators of the relation between PA and pain severity in people with CNCP, determine the quality of the studies, and examine potential publication bias.

2. Methods
This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. All methods and planned analyses were preregistered on the Open Science Framework (https://osf.io/5up34). All materials for this study, including analytic script, data, and record of deviations from this preregistered protocol can be found on the associated project page (https://osf.io/ukvu8/).

2.1. Data sources and searches
MEDLINE (PubMed), PsyCINFO, and CINAHL databases were searched electronically from inception to March 21, 2017. An updated search was performed (from April 7, 2017, through September 24, 2018) to include research from gray literature sources (ProQuest Dissertations and Theses, OLASTER, Open Grey, and PsyArXiv) and to identify new publications. All databases and gray literature sources were searched again on July 23, 2019, to capture additional relevant literature published between 2017 and 2019. Search terms for PA were searched again on July 23, 2019, to capture additional relevant literature published between 2017 and 2019. Search terms for PA used keywords drawn from prior reviews of health outcomes associated with PA, and included variations of happy, cheerful, joy, vigor, elated, enthusiastic, energetic interest, content, amused, humor, calm, relaxed, grateful, satisfied, positive affect, positive emotions, and positive mood. Search terms for chronic pain included variations of widespread pain, recurrent pain, persistent pain, and long-term pain. The details of the full search strategy are presented in eAppendix 1, http://links.lww.com/PAIN/A959.

2.2. Eligibility criteria and study selection
Studies were eligible for inclusion if they met the following criteria: (1) the study design was observational, experimental, or intervention (eg, randomized controlled trial); (2) participants were adults (18 years or older) with CNCP (12 weeks or more in duration); and (3) results were reported in sufficient quantitative detail to discern a directional effect of PA on pain severity. For all intervention studies, data from the baseline to first follow-up were included, with the baseline vs first follow-up contrast serving as the primary outcome. In the case of 2 or more groups receiving different PA interventions within one study, all were independently included.

Articles were excluded if they: (1) were not an empirical study; (2) did not involve human subjects; (3) did not include a measure of PA or a positive mood manipulation (eg, humorous films, pleasant images); (4) used a reversed indicator of negative affect (NA) as a measure of PA (eg, hopelessness vs hopefulness; pessimism vs optimism; fatigue vs vigor/vitality); (5) did not include a subjective or objective measure of pain severity; (6) assessed affect only in regard to a specific life experience (eg, “How happy are you about being pregnant?”); (7) examined only the directional effect of pain on PA or mean differences in PA between pain-impaired and non-impaired samples; (8) did not enroll individuals identified as suffering from chronic pain; (9) assessed acute or experimentally induced pain; (10) did not use an eligible study design; (11) did not examine or report a directional effect of PA on pain; (12) exclusively used a sample of patients with a primary cancer diagnosis; (13) were published in languages other than English; (14) did not include adults (aged 18 years and above); (15) exclusively used a sample of patients presenting with a primary psychological disorder; (16) did not directly target PA; (17) did not include sufficient quantitative information on study outcomes; (18) full text of article could not be located; or (19) were a duplicate identified during full-text screening. When possible, we also contacted authors for further information.

After duplicates were removed, titles and abstracts were screened by 2 independent reviewers (K.R. and K.G.) to determine whether the citation met eligibility criteria. Subsequently, 2 independent authors (A.D.O. and F.T.) assessed the full text of potentially eligible studies for inclusion. Conflicts were resolved by consensus. Figure 1 presents the study selection process and indicates the number of articles excluded at each phase of screening.

2.3. Data extraction and quality assessment
Two reviewers (A.D.O. and F.T.) independently extracted study characteristics and outcome data from published articles. Risk of bias was independently assessed by 2 reviewers (A.D.O. and F.T.) using the Effective Public Health Practice Project (EPHPP) tool. Specifically, the included studies were assessed for (1) selection bias, (2) study design, (3) confounders, (4) blinding, (5) data collection, and (6) withdrawals/dropouts. Each domain was rated as strong, moderate, or weak, and domain scores were averaged to provide a global rating for each study (interrater reliability 88%, Cohen’s kappa 0.79). Discrepancies were resolved by consensus.

2.4. Data synthesis and analysis
Meta-analyses were performed using the metafor and meta packages in R, version 3.4.3 (R Project for Statistical Computing). For each study, individual effect sizes were calculated within each independent sample. For observational studies (ambulatory and longitudinal), standardized regression coefficients were extracted and used as an effect size index. For experimental and intervention studies, effects sizes (Hedges’ g) were extracted from descriptive statistics. Similar to Cohen’s d, Hedges’ g effect sizes of 0.00 to 0.32 can be considered as small, effect sizes of 0.33 to 0.55 as moderate, and effect sizes of 0.56 to 1.20 as large. Although effect sizes were computed separately for each of the 3 study designs (observational, experimental, and intervention), we also computed an overall effect size $r_{\text{equivalent}}$ from exact t-values reported across studies. Specifically, we report $r_{\text{equivalent}}$, effect sizes on the Fisher Z-transformed metric, and used a standard error, as suggested by Rosenthal and Rubin, defined as the square root of N–3. Meta-analyses yielded a point estimate, confidence interval, and P-value, along with statistics for heterogeneity (assessed using the Cochran Q-statistic and the Higgins–Thompson I² values). Publication bias was evaluated using the Egger test (with $P < 0.10$ indicating asymmetry), and visual inspection of funnel plots. For completeness, we conducted p-curves (the distribution of statistically significant P values for a set of findings, with right-skewed p-curves suggesting findings that contain evidentiary value) and p-uniform test (a publication bias test based on the effect size in a set of studies).

2.5. Subgroup analyses
A priori subgroup analyses were performed to explore moderators of the PA-pain severity relation, including (1) risk of bias quality...
rating: weak, moderate, and strong; (2) demographics: percentage female, percentage racial minority, and mean age; (3) chronic pain status: fibromyalgia, rheumatoid arthritis, osteoarthritis, back pain, and multiple; (4) PA measurement: state and trait; and (5) covariate adjustment: unadjusted NA and adjusted NA. For categorical moderators that explained significant variance in the effect sizes (i.e., \( P < 0.05 \) for \( Q_M \)), post hoc contrasts were performed to determine which groups were statistically different. For continuous moderators, meta-regression analyses were used to determine whether variation in the effect sizes was explained by the moderator. A false discovery rate (FDR) type I error control was used for all comparisons to correct for multiple testing. 8

### 3. Results

#### 3.1. Study characteristics

From a total of 3063 retrieved articles, 151 were identified based on title and abstract screening for full-text review. Of these, 38 studies fulfilled eligibility criteria and were included in the systematic review. Descriptive details of the studies are presented in Table 1. The included studies were published between 1981 and 2018, came from 10 countries, with 25 studies from the United States; had sample sizes ranging from 8 to 360, and included a total of 4229 participants (mean [SD] age was 54 [9.57] years and 76% were women). It should be noted that not all studies reported the exact age or number of non-White participants.

Among the 38 included studies, 11 were observational (8 ambulatory and 3 longitudinal studies); 9 were experimental, and 18 were interventions. Among observational studies, the majority used self-report adjective ratings of positive valence (e.g., active, energetic, happy, cheerful, and joyful) to assess level of PA. State levels (momentary and daily) of PA were typically assessed in ambulatory studies, whereas trait levels (global ratings) of PA were typically measured in longitudinal studies. Among experimental studies, examples of PA-based inductions included viewing emotionally evocative images, humorous film clips, and guided imagery. Finally, in the
Table 1

Descriptive characteristics of the included studies.

<table>
<thead>
<tr>
<th>Source [country]</th>
<th>Year</th>
<th>Study type</th>
<th>Risk of bias</th>
<th>Sample size</th>
<th>Mean age</th>
<th>% White</th>
<th>% Female</th>
<th>Pain condition</th>
<th>PA manipulation/Measure</th>
<th>Pain outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arnold et al. 1 [Germany]</td>
<td>2008</td>
<td>E</td>
<td>W</td>
<td>120</td>
<td>49</td>
<td>—</td>
<td>83 M</td>
<td>Mood induction procedure using the IAPS; PANAS</td>
<td>Pain intensity using NRS</td>
<td></td>
</tr>
<tr>
<td>Baird et al. 3 [United States]</td>
<td>2006</td>
<td>I</td>
<td>S</td>
<td>28</td>
<td>73</td>
<td>—</td>
<td>100 O</td>
<td>GIR; mood measured as a subscale of HRQOL</td>
<td>Pain frequency and intensity using NRS</td>
<td></td>
</tr>
<tr>
<td>Basler et al. 5 [Germany]</td>
<td>1997</td>
<td>I</td>
<td>S</td>
<td>76</td>
<td>49</td>
<td>—</td>
<td>76 B</td>
<td>CBT</td>
<td>Pain intensity using NRS</td>
<td></td>
</tr>
<tr>
<td>Baxter et al. 6 [New Zealand]</td>
<td>2012</td>
<td>I</td>
<td>M</td>
<td>8</td>
<td>55</td>
<td>—</td>
<td>50 B</td>
<td>Character strengths and gratitude intervention; DESP; OHQSF</td>
<td>Pain intensity using VAS</td>
<td></td>
</tr>
<tr>
<td>Behrouz et al. 7 [Iran]</td>
<td>2017</td>
<td>I</td>
<td>M</td>
<td>55</td>
<td>74</td>
<td>—</td>
<td>71 M</td>
<td>Humor therapy</td>
<td>Pain intensity using BPI (modified German version)</td>
<td></td>
</tr>
<tr>
<td>Carson et al. 10 [United States]</td>
<td>2005</td>
<td>I</td>
<td>M</td>
<td>43</td>
<td>51</td>
<td>63</td>
<td>61 B</td>
<td>Loving-kindness meditation</td>
<td>Pain intensity and pain rating index using MPQ; usual and worst pain using BPI</td>
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</tr>
<tr>
<td>Connelly et al. 16 [United States]</td>
<td>2007</td>
<td>A</td>
<td>W</td>
<td>94</td>
<td>56</td>
<td>91</td>
<td>72 R</td>
<td>PANAS</td>
<td>Pain intensity using VAS</td>
<td></td>
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<tr>
<td>Davis and Zautra 20 [United States]</td>
<td>2013</td>
<td>I</td>
<td>M</td>
<td>79</td>
<td>46</td>
<td>83</td>
<td>98 F</td>
<td>MB intervention targeting socioemotional regulation; PANAS</td>
<td>Daily pain intensity and coping using NRS</td>
<td></td>
</tr>
<tr>
<td>Davis et al. 19 [United States]</td>
<td>2014</td>
<td>E</td>
<td>M</td>
<td>110</td>
<td>57</td>
<td>91</td>
<td>100 M</td>
<td>Positive and neutral mood induction; PANAS-X</td>
<td>Clinical pain using NRS</td>
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<tr>
<td>Dowd et al. 23 [Ireland]</td>
<td>2015</td>
<td>I</td>
<td>W</td>
<td>124</td>
<td>44</td>
<td>—</td>
<td>90 M</td>
<td>MBCT with emphasis on emotional regulation; SLS; MAAS</td>
<td>Pain intensity and interference using BPI</td>
<td></td>
</tr>
<tr>
<td>Finan et al. 27 [United States]</td>
<td>2009</td>
<td>A</td>
<td>W</td>
<td>260</td>
<td>57</td>
<td>88-93</td>
<td>100 M</td>
<td>PANAS</td>
<td>Daily average pain using NRS</td>
<td></td>
</tr>
<tr>
<td>Finan et al. 29 [United States]</td>
<td>2013</td>
<td>A</td>
<td>W</td>
<td>151</td>
<td>61</td>
<td>62</td>
<td>68 O</td>
<td>PANAS-X; POMS - Bipolar</td>
<td>Pain severity using WOMAC</td>
<td></td>
</tr>
<tr>
<td>Fors and Götestam 30 [Norway]</td>
<td>2000</td>
<td>I</td>
<td>M</td>
<td>58</td>
<td>46</td>
<td>—</td>
<td>100 F</td>
<td>Gl</td>
<td>Pain intensity using VAS</td>
<td></td>
</tr>
<tr>
<td>Garland et al. 34 [United States]</td>
<td>2014</td>
<td>I</td>
<td>S</td>
<td>115</td>
<td>48</td>
<td>65</td>
<td>68 M</td>
<td>MB, CBT</td>
<td>Pain intensity and interference using BPI</td>
<td></td>
</tr>
<tr>
<td>Garland et al. 32 [United States]</td>
<td>2017</td>
<td>I</td>
<td>W</td>
<td>55</td>
<td>49</td>
<td>75</td>
<td>62 M</td>
<td>MB, CBT</td>
<td>Pain intensity using NRS</td>
<td></td>
</tr>
<tr>
<td>Gruszczynska et al. 36 [Poland]</td>
<td>2015</td>
<td>A</td>
<td>W</td>
<td>95</td>
<td>51</td>
<td>—</td>
<td>100 R</td>
<td>Folkman &amp; Lazarus PA Scale</td>
<td>Daily pain using VAS</td>
<td></td>
</tr>
<tr>
<td>Guillory et al. 37 [United States]</td>
<td>2015</td>
<td>I</td>
<td>M</td>
<td>68</td>
<td>49</td>
<td>63</td>
<td>75 M</td>
<td>Social support text messaging intervention; PAM</td>
<td>Pain intensity and interference using NRS</td>
<td></td>
</tr>
<tr>
<td>Hausmann et al. 41 [United States]</td>
<td>2017</td>
<td>I</td>
<td>S</td>
<td>42</td>
<td>68</td>
<td>57</td>
<td>17 O</td>
<td>PPI; PANAS; SLS</td>
<td>Pain severity and functional difficulty using WOMAC</td>
<td></td>
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<tr>
<td>Hausmann et al. 39 [United States]</td>
<td>2018</td>
<td>I</td>
<td>S</td>
<td>360</td>
<td>64</td>
<td>50</td>
<td>24 O</td>
<td>PPI; International PANAS-SF; SLS</td>
<td>Pain severity and functional difficulty using WOMAC</td>
<td></td>
</tr>
<tr>
<td>Herrero et al. 44 [Spain]</td>
<td>2014</td>
<td>E</td>
<td>S</td>
<td>40</td>
<td>49</td>
<td>—</td>
<td>100 F</td>
<td>Virtual reality; mood state using VAS; mood intensity using NRS</td>
<td>Pain intensity using NRS</td>
<td></td>
</tr>
<tr>
<td>Kamping et al. 47 [Germany]</td>
<td>2013</td>
<td>E</td>
<td>S</td>
<td>32</td>
<td>52</td>
<td>—</td>
<td>100 F</td>
<td>Mood induction procedure using the IAPS</td>
<td>Pain intensity using VAS</td>
<td></td>
</tr>
<tr>
<td>Kruszweski 52 [United States]</td>
<td>2010</td>
<td>A</td>
<td>W</td>
<td>143</td>
<td>58</td>
<td>89</td>
<td>100 M</td>
<td>PANAS</td>
<td>Average daily pain using NRS</td>
<td></td>
</tr>
<tr>
<td>Litt et al. 55 [United States]</td>
<td>2004</td>
<td>A</td>
<td>W</td>
<td>30</td>
<td>36</td>
<td>80</td>
<td>87</td>
<td>TMD</td>
<td>PANAS; Circumplex model of mood</td>
<td>Pain intensity using NRS</td>
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<tr>
<td>McKee 56 [United States]</td>
<td>1981</td>
<td>E</td>
<td>M</td>
<td>20</td>
<td>36</td>
<td>90</td>
<td>50 M</td>
<td>GIR</td>
<td>Pain intensity using NRS</td>
<td></td>
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<tr>
<td>Mun et al. 61 [United States]</td>
<td>2017</td>
<td>A</td>
<td>W</td>
<td>220</td>
<td>51</td>
<td>78</td>
<td>87 R</td>
<td>Shortened PANAS</td>
<td>Overall daily pain intensity using NRS</td>
<td></td>
</tr>
<tr>
<td>Müller et al. 60 [United States]</td>
<td>2016</td>
<td>I</td>
<td>M</td>
<td>96</td>
<td>59</td>
<td>96</td>
<td>70 O</td>
<td>Tailored PPI; PANAS; PWI-A</td>
<td>Pain severity using NRS</td>
<td></td>
</tr>
</tbody>
</table>
intervention research reported here, a variety of methods were used to increase PA in people with CNCP, including expressing thanks, practicing acts of kindness, and savoring positive moments, among others.39

### 3.2. Risk of bias

The assessment of the quality of the study methodology for the 5 domains (selection bias, study design, confounders, blinding, and data collection) is reported in eFigure 1 in the Supplement (available at http://links.lww.com/PAIN/A959). Risk-of-bias assessments for individual studies included in the qualitative review are summarized in Table 1. Following the EPHPP tool, 8 studies1144 were classified as “strong” or having low risk of bias; 13 studies6,7,10,19,20,30,37,58,60,72,77,84,92 (44.74%) were categorized as “weak” or having high risk of bias. Weakness ratings derived from the inadequate control of confounders and insufficient information regarding study design, as well as lack of blinding.

<table>
<thead>
<tr>
<th>Source [country]</th>
<th>Year</th>
<th>Study type</th>
<th>Risk of bias</th>
<th>Sample size</th>
<th>Mean age</th>
<th>% White</th>
<th>% Female</th>
<th>Pain condition</th>
<th>PA manipulation/Measure</th>
<th>Pain outcome</th>
</tr>
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<tbody>
<tr>
<td>Peters et al.65 [The Netherlands]</td>
<td>2017</td>
<td>I</td>
<td>S</td>
<td>284</td>
<td>49</td>
<td>—</td>
<td>85</td>
<td>F</td>
<td>Internet-based PPI; present happiness using NRS; SCS-SF; BMIS</td>
<td>Pain intensity using NRS</td>
</tr>
<tr>
<td>Pintard67 [United States]</td>
<td>1986</td>
<td>E</td>
<td>W</td>
<td>60</td>
<td>52</td>
<td>77</td>
<td>65</td>
<td>M</td>
<td>Humor induction; HA; POMS; CHS</td>
<td>Present pain intensity and pain rating index MPO</td>
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<tr>
<td>Potter68 [United States]</td>
<td>1999</td>
<td>L</td>
<td>W</td>
<td>285</td>
<td>63</td>
<td>—</td>
<td>100</td>
<td>M</td>
<td>PANAS</td>
<td>Aggregate of average level of pain over the past week</td>
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<tr>
<td>Raft et al.72 [United States]</td>
<td>1986</td>
<td>E</td>
<td>M</td>
<td>52</td>
<td>—</td>
<td>85</td>
<td>60</td>
<td>M</td>
<td>Pleasant imagery task</td>
<td>Pain intensity using VAS</td>
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<tr>
<td>Seebach et al.76 [United States]</td>
<td>2012</td>
<td>L</td>
<td>W</td>
<td>141</td>
<td>59</td>
<td>81</td>
<td>58</td>
<td>B</td>
<td>PANAS</td>
<td>Pain intensity using BPI</td>
</tr>
<tr>
<td>Shayan et al.77 [Germany]</td>
<td>2017</td>
<td>I</td>
<td>M</td>
<td>88</td>
<td>53</td>
<td>—</td>
<td>67</td>
<td>M</td>
<td>Visual stimuli (e.g., pictures of loved ones, landscapes); valence and arousal using SAM</td>
<td>Average pain intensity using NRS</td>
</tr>
<tr>
<td>Strand et al.80 [Norway]</td>
<td>2007</td>
<td>L</td>
<td>W</td>
<td>163</td>
<td>50</td>
<td>—</td>
<td>79</td>
<td>M</td>
<td>PANAS</td>
<td>Past week’s average pain using NRS</td>
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<tr>
<td>Tse et al.84 [Hong Kong]</td>
<td>2010</td>
<td>I</td>
<td>M</td>
<td>70</td>
<td>79</td>
<td>—</td>
<td>54</td>
<td>M</td>
<td>Humor therapy; SHS; Revised LSI-A</td>
<td>Cantonese VRS</td>
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<tr>
<td>Wilkinson81 [United States]</td>
<td>2003</td>
<td>E</td>
<td>S</td>
<td>60</td>
<td>—</td>
<td>—</td>
<td>75</td>
<td>M</td>
<td>SHRQ</td>
<td>Current pain rating and location using NRS</td>
</tr>
<tr>
<td>Willmarth82 [United States]</td>
<td>1998</td>
<td>E</td>
<td>M</td>
<td>96</td>
<td>45</td>
<td>—</td>
<td>41</td>
<td>M</td>
<td>Hypnotically induced positive mood</td>
<td>Sensory, affective, and overall global pain ratings via VAS</td>
</tr>
<tr>
<td>Zautra et al.84 [United States]</td>
<td>2001</td>
<td>A</td>
<td>W</td>
<td>175</td>
<td>64</td>
<td>96</td>
<td>100</td>
<td>M</td>
<td>PANAS</td>
<td>Average past week pain using NRS</td>
</tr>
<tr>
<td>Zautra et al.85 [United States]</td>
<td>2008</td>
<td>I</td>
<td>S</td>
<td>144</td>
<td>52</td>
<td>89</td>
<td>68</td>
<td>R</td>
<td>CBT; MB intervention targeting emotion regulation and adaptation; PANAS</td>
<td>Average daily pain using NRS</td>
</tr>
</tbody>
</table>

### 3.3. Meta-analyses

A total of 29 studies (N = 3521) fulfilled the eligibility criteria and were included in the final meta-analyses.6,7,10,19,20,23,29,30,32,34,36,39,41,44,52,58,60,61,65,68,72,76,77,80,84,86,91,94,95 Pooling the results of the 29 studies, an average 

$$r = 0.23$$

(95% CI = −0.36 to −0.13; P < 0.0001) was observed between PA and chronic pain severity.

#### 3.3.1. Observational studies

Eight observational studies39,66,67,68,69,70,71,72,73,74 were included in the primary analysis, totaling 1482 participants. Figure 2 displays the forest plots for the meta-analyses of the association between PA and pain severity in this group of studies. Positive effect was associated with decreased chronic pain severity (β = −0.13, z = −4.60, P < 0.001), but heterogeneity across studies was substantial ($I^2 = 89.25$%; 95% CI 73.6-96.3; Qe (13) = 84.69, P < 0.001), indicating significant variation in the effect sizes. The Egger test for funnel plot asymmetry yielded a result significant at the 0.10 level (z = −1.78, P = 0.08). However, the funnel plot
Supplement (available at http://links.lww.com/PAIN/A959). The shape of the p-curve was significantly right-skewed ($z = -9.23, P < 0.001$), indicating that the set of studies contains evidentiary value.

### 3.3.2. Experimental studies

Five experimental studies\(^{19,44,58,72,91}\) provided data on pain severity for 282 participants. Contrary to expectations, PA was not associated with pain severity in experimental studies (Hedges' $g = -1.02; Z = -1.55; P = 0.12$). Heterogeneity was significant and high ($I^2 96.1\%; 95\% CI 87.3-99.6; Q_E (4) = 33.87, P < 0.001$), and funnel plots (eFigure 4 in the Supplement, available at http://links.lww.com/PAIN/A959) and the Egger test ($z = -5.18, P < 0.0001$) suggested asymmetry. Likewise, the p-uniform* test yielded a significant result ($L_{pb} = 5.83, P = 0.05$), indicating the likely presence of publication bias. As shown in the forest plot in Figure 3, there were 2 studies with small sample sizes but relatively large effect sizes,\(^{48,72}\) whereas the larger studies all had effect sizes that were much closer to zero. eFigure 5 in Supplement (available at http://links.lww.com/PAIN/A959) reports the observed p-curve for experimental studies, which was significantly right-skewed ($z = -10.1, P < 0.001$), suggesting that the set of significant findings contains evidentiary value.

### 3.3.3. Intervention studies

Sixteen intervention studies\(^{5,7,10,20,23,30,32,34,37,39,41,60,65,77,84,95}\) provided data on pain severity for 1757 participants. As shown in Figure 4, PA was inversely associated with chronic pain severity (Hedges' $g = -0.36; Z = -3.54; P < 0.001$). Heterogeneity was high ($I^2 73.8\%; 95\% CI 52.6-90.1; Q_E (17) = 59.53, P < 0.001$), and funnel plots (eFigure 6 in the Supplement, available at http://links.lww.com/PAIN/A959) and the Egger test ($z = -2.34, P = 0.02$) suggested potential asymmetry. However, the p-uniform* test yielded a nonsignificant result ($L_{pb} = 0.31, P = 0.86$), indicating lack of evidence for publication bias. eFigure 7 in the Supplement (available at http://links.lww.com/PAIN/A959) reports the observed p-curve for experimental studies, which was significantly right-skewed ($z = -9.69, P < 0.001$), suggesting that the set of significant findings contains evidentiary value.

### 3.4. Subgroup and exploratory analyses

A priori subgroup analyses within observational and intervention studies are shown in eTables 1 to 2 for categorical moderators and eTables 3 to 4 for continuous moderators (see Supplement, available at http://links.lww.com/PAIN/A959). Subgroup analyses were not conducted on experimental studies due to the small number of studies in this cluster. With respect to the categorical moderators, lower effect sizes were found for observational studies that adjusted for NA ($\beta = -0.09; Z = -2.91; P = 0.003$) compared to those that did not ($\beta = -0.18; Z = -4.39; P < 0.0001$); however, the difference between effect sizes did not reach conventional levels of statistical significance, $Q_M = 3.52, P = 0.06$. For continuous moderators, the gender composition of the sample moderated the relation between PA and chronic pain severity, such that observational study samples with a higher proportion of female participants reported larger effect sizes on average, $Q_M = 22.68, P < 0.0001$. Finally, larger effect sizes were found in intervention studies with older compared with younger samples, $Q_M = 5.82, P = 0.015$. This moderating effect, however, became nonsignificant after FDR correction, $P = 0.125$.

Post hoc exploratory analyses were conducted to examine intervention studies that reported data on the magnitude of change in PA ($n = 6$) and average rates of depression in the sample ($n = 5$). Among the included studies, effect sizes did not differ significantly as a function of reported PA change, $Q_M = 0.05, P = 0.823$. Studies reporting higher rates of depression had effect sizes that were not significantly different compared to those reporting lower rates of depression, $Q_M = 0.17, P = 0.680$.

### 4. Discussion

#### 4.1. Main findings

This systematic review and meta-analysis provides quantitative evidence that PA is associated with reduced pain severity among adults with CNCP. Previous narrative reviews\(^{28,38,57}\) have reported links between PA and pain. In the present review, we
undertook a meta-analysis of observational, experimental, and intervention studies, enabling the quantification of these links and the exploration of key sources of heterogeneity across studies. Pooling the results of 29 observational, experimental, and interventions studies, we found an average \( r \)-effect size of \(-0.23\) between PA and pain severity among people with CNCP. This effect size is similar to the effect size between PA and acute physical pain \((r = -0.18)\) found by Kushlev et al.,\(^{53}\) and smaller than the effect size reported by Howell et al.\(^{45}\) in their meta-analyses examining the effects of laboratory-induced PA on pain tolerance \((r = 0.32)\).

Effect sizes were relatively small in intervention studies \((g = -0.36)\). This finding is in line with 2 previous meta-analyses of RCTs on the effects of PA-based interventions on other pain-relevant outcomes, including depression and anxiety. Hendriks et al.\(^{43}\) reported relatively small effects on these outcomes \((g = -0.35\) to \(-0.39)\), and a recent meta-analysis by Chakhssi et al.\(^{12}\) conducted among clinical samples with psychiatric or somatic disorders also reported small effects for depression \((g = -0.23)\) and anxiety \((g = -0.36)\), respectively. Within observational studies, a small significant effect size of \(-0.13\) was found between PA and chronic pain severity. The magnitude of this effect is similar to that found in a prior meta-analysis examining the association between NA-based predictors (eg, fear avoidance) and pain intensity.\(^{51}\)

In addition, we examined the impact of categorical (risk of bias, chronic pain status, state vs trait PA measurement, and NA adjustment) and continuous moderators (age, gender, and race). Subgroup analyses found three significant moderators. Notably, PA was associated with lower chronic pain severity in observational studies that adjusted for NA and had a higher percentage of female vs male participants. In addition, within intervention studies, age moderated the link between PA and pain severity, with larger effect sizes evident in studies with older compared with younger samples. Finally, in exploratory analyses, neither reported change in PA nor depression composition was found to significantly moderate the relation between PA and chronic pain severity.

### 4.2. Strengths and limitations

There are several strengths to this review, including its preregistered design, comprehensive search strategy, systematic study inclusion, thorough assessment of study quality, use of a priori subgroup analyses, and formal tests for heterogeneity \((Q\text{-statistic}; I^2)\) and publication bias \((p\text{-curve} \text{ and } p\text{-uniform}^*)\). There are also limitations to our review. First, although inspection of the funnel plot and the Egger test did not identify strong evidence of publication bias in any of our analyses, we found high heterogeneity in terms of study population. Second, although moderating analyses revealed mainly nonsignificant associations, the small number of studies within each cluster prevented us from performing high-powered subgroup analyses.\(^{96}\) Third, study quality did not
prove to be a significant moderator of the PA-pain effect sizes. However, it is possible that our risk assessment instrument did not adequately capture the range of biases inherent in different types of study designs (eg, observational, experimental, and intervention studies). That is, we assigned quality ratings based on an overall assessment of risk; however, an alternative approach would be to use design-specific criteria to assess common sources of bias specific to certain types of study designs.

Fourth, only a small number of experimental (n = 2) and intervention studies (n = 6) reported data on the magnitude of change in PA, thus leaving unanswered the question of whether PA is the active psychological component in the causal chain. Thus, it is critical that researchers report data on the magnitude of change in the primary outcome (ie, PA) as a means of assessing the efficacy of experimental and intervention procedures. Such data can then be used as sample-specific moderators in subsequent meta-analyses of PA-pain effect sizes. Likewise, fewer observational studies (n = 2 ambulatory; n = 3 longitudinal) examined relationships between PA and chronic pain severity while controlling for measures of NA. An important methodological issue in studies of PA and health is whether relationships are independent of negative affective states. In subgroup analyses, we found marginally lower effect sizes in observational studies that adjusted for NA compared to those that did not. However, with such a small number of studies, definitive conclusions cannot be drawn. Similarly, few of the included intervention studies (n = 5) assessed rates of depression. It is known that depression is highly comorbid with the occurrence of chronic pain, and there is some evidence that depression may be an important moderator of interventions targeting PA regulation in chronic pain patients.

Given the limited number of studies reporting on depression, firm conclusions on the effects of PA-enhancing interventions on chronic pain severity among clinical populations cannot yet be made. Fifth, the current meta-analysis focused on pain severity as the primary outcome, but the effects of PA on other salient outcomes (eg, pain interference and pain catastrophizing) in people with CNCP need to be established in future research. Finally, despite the inclusion of gray literature, we used English search terms, which may have prevented us from identifying relevant studies published in other languages.

4.3. Implications for research and practice

Our findings support guideline recommendations that encourage clinicians to consider psychological treatments in the care of patients with CNCP, particularly interventions that have a PA component. Nevertheless, it is unclear whether existing nonpharmacological treatments for CNCP that incorporate elements of PA enhancement (eg, MBSR; acceptance and commitment therapy; and emotional awareness and expression therapy) are sufficient in reducing pain severity or whether the efficacy of these treatments to boost PA can be further strengthened. An additional critical question is whether psychological treatments for CNCP that promote PA have greater benefits than those that are aimed at reducing NA. There is evidence that treatment modalities that incorporate mindfulness-based strategies (eg, relaxation and presence-focused awareness) may be an effective treatment alternative to standard CBT. However, as Finan et al. have noted, treatment approaches for CNCP such as CBT, acceptance and commitment therapy, and MBSR typically emphasize minimizing negative thoughts and emotions associated with pain. As a consequence, it is currently unclear which therapeutic mechanisms (PA-enhancing or NA-reducing strategies) should be optimized in existing psychosocial treatments for CNCP. Finally, it also may be possible that interventions that integrate both PA-based and NA-based strategies could augment the therapeutic impact of current empirically supported treatments for CNCP.

5. Conclusion

To the best of our knowledge, this is the first preregistered systematic review and meta-analysis to examine the association between PA and pain severity in adults with CNCP. The results indicated that PA is associated with a modest decrease in pain severity across observational, experimental, and intervention studies. The findings suggest that among adults with CNCP, PA may be a factor that promotes resilience in the face of chronic pain.

Conflict of interest statement

The authors have no conflicts of interest to declare.

Appendix A. Supplemental digital content

Supplemental digital content associated with this article can be found online at http://links.lww.com/PAIN/A959.

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