Title:

Distinct multidimensional anger profiles predict current and long-term chronic pain outcomes

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Number of figures: 3

Number of Tables: 7

Abstract

Anger is prevalent in chronic pain (CP), often co-occurring with heightened distress and disability. The complexity of the anger construct manifests in heterogeneity of how anger is experienced, expressed, and regulated. Nevertheless, most work does not consider the inter-relationships between multiple dimensions of anger, limiting understanding of how anger might differentially contribute to pain outcomes. Here, various anger metrics and latent profile analysis (LPA) were utilized to identify disparate anger profiles in people with CP. Whether these profiles associated cross-sectionally and longitudinally with pain outcomes was subsequently examined. Data was collected from 735 treatment-seeking adult patients with CP of varied etiologies, of which 242 also completed follow-up assessments about 5 months after baseline. Anger measures included state and trait anger, anger expression (anger-in, anger-out), anger control (control-in, control-out), and perceived injustice. Pain outcomes included pain- intensity, distribution, interference, and behavior, and physical function. LPA identified four distinct anger profiles characterized by the combination of varying levels (low, medium, high) of anger and of perceived injustice. These profiles significantly associated with pain outcomes at both baseline and follow-up, above and beyond anxiety and depression. Profiles with medium-to-high levels of both anger (state, trait, and expression) and perceived injustice predicted the worst pain outcomes, suggesting that injustice-based profiling should be prioritized for anger-related stratification of risk in CP. The mechanistic and prognostic value of these anger profiles suggests that early assessment could enhance long-term treatment planning and advance personalized pain care, further emphasizing the need for tailored, anger-focused, patient-specific interventions.

Perspectives*:* This study demonstrates that multidimensional anger profiles, particularly those marked by higher perceived injustice, are linked to more severe and persistent high impact chronic pain. Identifying these profiles may facilitate early clinical screening for at-risk patients, personalized emotion-focused interventions, and potentially prevent progression to high-impact chronic pain and long-term disability.

Keywords:

Anger; Chronic Pain; Latent Profile Analysis; High Impact Chronic Pain; Perceived Injustice

Distinct multidimensional anger profiles predict current and long-term chronic pain outcomes

The complexity of chronic pain (CP) extends beyond physical symptoms and functional disability to impact social and psychological domains, and overall quality of life[1]. Moreover, emotional factors seem to critically shape CP outcomes, influencing symptom severity and patients' coping abilities[2–4].

Among emotions linked to CP, anger is particularly salient[5], with about 70% of patients frequently experiencing anger[6]. Anger is not a unidimensional construct; instead, it encompasses elements such as *state anger* (transient emotional reactions), *trait anger* (a stable tendency toward anger), various modes of expression, such as *anger-in* (suppressed anger) and *anger-out* (externalized anger) and various regulation modes of both the experience and expression of anger, also referred to as *anger control*[7–10]. Research has consistently shown that heightened anger in CP, whether in its state, trait, or expressive forms, is associated with worsened pain outcomes, including greater pain intensity, heightened negative emotional experiences, and increased disability, which restricts social participation and diminishes overall quality of life[11–13]. Recently, perceived injustice – an anger-related cognitive factor defined by maladaptive appraisals of unfair treatment and irreparable loss[14] – has been linked to greater distress, higher pain, and impaired coping capabilities[15].

Despite growing recognition of the multidimensional nature of anger, most research, especially in CP, focuses on isolated components, without fully examining the interplay between various anger dimensions. This approach simplifies anger's role in CP, and neglects the possibility that distinct combinations of anger dimensions may have differential effects on pain-related outcomes[9,16]. A recent systematic review and meta-analysis[11] highlights the complexity of the interaction between anger and pain, revealing, for example, that state anger, which fluctuates with situational variability, is closely linked to moment-to-moment pain

experiences, while anger-in is more strongly associated with pain-related disability. Identifying disparate multidimensional-based anger profiles could enable clinicians to tailor psychosocial interventions to specific patient subgroups, thereby improving patient outcomes.

Therefore, the present study sought to move beyond examining isolated dimensions of anger towards examining the complex interrelationships between several dimensions of anger, in CP. To this end, latent profile analysis (LPA)[17] was utilized to identify distinct underlying profiles of anger in treatment-seeking adults with CP, and examined how these profiles relate to key pain-related outcomes. LPA, a data-driven, person-centered statistical approach, was used to uncover clinically meaningful subgroups based on unique combinations of state and trait anger, anger expression (anger-in and anger-out), anger control (control-in and control-out), and perceived injustice. This approach represents a crucial step toward advancing precision medicine in CP by enabling more targeted psychological assessments and interventions. We hypothesized that distinct anger profiles would emerge and that these profiles would (i) capture meaningful heterogeneity in anger dimensions within a CP population, (ii) be associated with variability in pain-related outcomes at baseline, above and beyond the emotional factors of anxiety and depression, and (iii) predict pain outcomes over time. By incorporating both cross-sectional and longitudinal analyses, the study addresses a key gap in the literature – namely, the absence of empirically derived anger typologies that capture the dynamic and multidimensional role of anger in CP.

Methods

General Procedure and Participants

Data was collected from patients receiving care at the Stanford Pain Management Centers. Patients completed surveys as part of their routine clinical care via Stanford University's

CHOIR[a]. CHOIR is a learning health system administering electronic surveys assessing self-reported demographic information, pain characteristics, and multiple domains of health status in real-world clinical settings[18–20]. Survey completion is encouraged, but not mandatory, thus patients may choose not to respond to certain items or assessments. The health status assessments are mostly based on the National Institute of Health's Patient-Reported Outcomes Measurement Information System (PROMIS)[21,22]. Using computerized adaptive testing allows for automatically selecting only a subset of items from each PROMIS item bank until resulting measurements meet preset criteria for standard errors[23]. Typically, no more than eight items are selected, though a minimum of 4 is required. PROMIS items are commonly rated on a 5-point frequency scale ranging from 1 (never) to 5 (always). The raw sum scores are then transformed into standardized T-scores, where the mean (M) is 50 and represents the normative mean of the U.S. general population and the standard deviation (SD) is 10. Higher T scores represent more of the measured construct.

Between August 2018 and February 2019, patients were further presented with an additional optional survey to complete, which included the State-Trait Anger Expression Inventory version 2 (STAXI-2)[10] assessments (further details below). They were also informed that at the end of this additional survey, they will have the opportunity to enlist for a follow-up survey including the same assessments, which will be sent 3 months later. Patients were further informed that those completing the additional surveys will be included in a raffle for 100 gift cards of different values (10 of $50, 40 of $25, and 50 of $10). Collection of follow-up data stopped in August of 2019. These procedures were approved by the Stanford University School of Medicine Institutional Review Board (IRB). The IRB waived informed consent, as CHOIR data was collected for clinical care and quality improvement purposes.

[a] http://choir.stanford.edu

Neither patients nor public were involved in the study's conceptualization, design, conduct, or dissemination of results.

In all, baseline timepoint included 735 patients. Of these, 242 patients chose to complete the follow-up timepoint, with an average interval of 141±68 (M±SD) days between timepoints. An additional 52 patients at baseline and 3 patients at follow-up did not complete the additional survey and were excluded.

Anger assessments

State-like anger was assessed using the PROMIS Anger assessment[24]. This measure evaluates the respondent's frequency and intensity of feeling angry, in the past 7 days. Scores are represented in T-scores (see General Procedure and Participants section).

Trait anger was measured using the Trait Anger Scale, a component of the STAXI-2[10]. This subscale assesses the general disposition to experience anger, reflecting the individual's propensity to perceive situations as frustrating or annoying and to respond with anger over time. This scale includes ten items rated on a 4-point frequency scale ranging from 1 (almost never) to 4 (almost always). Scores are summed to produce a total score ranging from 10-40, with higher scores indicating a greater trait tendency to be angry.

Anger expression and anger control were assessed using the Anger Expression Inventory, also part of the STAXI-2[10]. These subscales evaluate how individuals typically express and control their anger, including anger-in (suppression), anger-out (expression), anger control-in (control of suppression), and anger control-out (control of outward expression). Each subscale consists of eight items rated on a 4-point frequency scale from 1 (almost never) to 4 (almost always). Scores are then summed to produce a total score ranging from 8-32, with higher scores indicating greater tendencies in that particular subscale.

Injustice experience was assessed using the Injustice Experience Questionnaire (IEQ)[25]. The IEQ measures the extent to which individuals perceive their medical condition as unjust, focusing on two dimensions: unfairness/blame and severity/irreparability of loss. The questionnaire consists of twelve items rated on a 5-point frequency scale from 0 (never) to 4 (all the time). Scores from the six items in each dimension are summed, ranging from 0 to 24, with higher scores indicating a stronger perception of injustice and attribution of blame (unfairness/blame subscale) or a heightened sense of severity and irreversibility of the loss associated with the health condition (severity/irreparability subscale).

Pain-related assessments

The *pain distribution in the body* was assessed using the CHOIR body map[26], a schema of the body divided into 74 symmetrical segments (36 on the front and 38 on the back). Participants marked the segments where they experienced pain. Both male and female versions of the body map were available; participants who did not specify their gender were given the female version by default. The total pain distribution was calculated by counting the number of marked segments, yielding a score from 0 to 74.

A composite score of *pain intensity* was calculated by averaging three self-reported measures for worst and average pain in the last 7 days and current pain. These measures used the common 0-10 Numerical Rating Scale (NRS), where 0 represents "no pain" and 10 indicates "the worst pain imaginable"[3,27]. *Pain duration* was determined based on the number of months since the onset of CP, as self-reported by the patients.

PROMIS-based instruments were utilized to measure *pain interference, pain behavior, and physical function*, including upper body and mobility tasks[24]. *Pain interference* assessed the extent by which pain hinders daily activities and impacts quality of life in the past 7 days, using a 5-point Likert scale from 1 (Not at all) to 5 (Very much). *Pain behavior* assessed the

frequency of observable pain-related actions (e.g., grimacing, guarding) in the past 7 days, using the same 5-point scale. *Physical function* was evaluated separately for ability to perform upper body and mobility tasks in the past 7 days, rated on a 5-point scale from 1 (Unable to do) to 5 (Without any difficulty). All scores are represented in T-scores (see General Procedure and Participants section).

Negative affect assessments

PROMIS-based instruments were also utilized to measure negative affect-related factors, namely *anxiety* and *depression*[24]. Each measure evaluates the frequency and intensity of anxious and depressive feelings experienced over the past 7 days, rated on a 5-point Likert scale ranging from 1 (Never) to 5 (Always). All scores are represented in T-scores (see General Procedure and Participants section).

Data Analysis

Latent Profile Analysis (LPA) was computed using MPlus ver. 8.4[28] to identify distinct anger profiles based on the anger measures at baseline. LPA is a data-driven person-centered mixture-model method frequently utilized to identify subtypes of homogeneous latent subgroups within a population[29,30]. This iterative technique aggregates similar response profiles to form distinct subgroups or classes of patient profiles. Latent profile solutions ranging from 2 to 5 profiles were tested to identify the best-fitting model. Model selection was guided by multiple fit indices, including the Akaike Information Criterion (AIC), Bayesian Information Criterion (BIC), sample size-adjusted BIC (SABIC), Lo-Mendell-Rubin adjusted likelihood ratio test (LRT), bootstrap likelihood ratio test (BLRT), profile size, and entropy[31–33]. AIC and BIC are information criteria used to compare model fit, with lower values indicating a better fit. Entropy, which ranges from 0 to 1, is considered acceptable when exceeding 0.80, indicating clear profile classification. Although there is no definitive

standard for profile size, profiles representing less than 5% of the sample may raise concerns about their validity due to limited representation. The LRT compares the current model to one with one fewer profile, with a non-significant result ($p > .05$) suggesting the simpler (most parsimonious) model is preferable. Ultimately, the selection of the final number of profiles was based on theoretical relevance and the interpretability of the profiles. Missing data were addressed using a maximum likelihood estimator, which is robust to data non-normality

A total of eight measures of anger were selected for inclusion in the LPA to provide a comprehensive overview of the multidimensional construct of anger. These measures encompass: state-like (PROMIS) anger, trait anger, anger expression out, anger expression in, anger control out, anger control in, and IEQ's severity/irreparability of loss, and unfairness/blame sub-scales.

Analysis of variance (ANOVA) were conducted using R[34] to examine differences in anger dimensions across profiles and to investigate the relationship between latent anger profiles and pain-related symptoms at baseline and follow-up. At baseline, a stepwise approach in the ANCOVA (analysis of covariance) models was employed to analyze the effect of anger profiles on pain outcomes, incrementally controlling for covariates. At first, the interaction between pain variables and anger profiles was tested, then progressively added sociodemographic factors (age, sex, education), clinical variables (pain duration), and negative affect covariates (anxiety, depression) across models. An exploration was conducted to consider which profiles are more likely to meet criteria for High Impact Chronic Pain (HICP)[35,36] by applying the established clinical threshold of a PROMIS Pain Interference T-score ≥ 65[37]. To test the relationship between anger profiles and HICP in more detail, the number and proportion of individuals with PROMIS-PI T-scores ≥ 65 within each profile was calculated and a chi-square test was conducted to assess differences across groups.

At follow-up, due to limited power, only the covariate "days between timepoints" was controlled for. Additionally, to explore whether there is a significant change between baseline and follow-up in pain outcomes depending on baseline anger profiles, analyses were conducted using the same subsample of participants (N=242) who provided responses at both baseline and follow-up[b]. An ANCOVAs was run with timepoints and anger profiles as factors, incorporating the number of days between timepoints as a covariate. Bonferroni correction was applied to all post hoc pairwise analyses to account for the number of multiple comparisons.

Results

Sample Characteristics

The majority of the sample were female (70.3%) adults (51.56 years old on average), and highly educated (18.20 years of education on average). Most identified as White (60.1%) and Non-Hispanic/Non-Latino (80.3%), and over half were living with a partner (58.64%). At follow-up, the sample characteristics remained similar (see Table 1).

Table 1. *Demographic characteristics of participants with CP at baseline and follow-up*. The data presented is based entirely on baseline information. Abbreviations: N – total sample size, n – subsample size, SD – standard deviation.

	All participants	**Participants who returned for the follow-up**
N	735	242
Sex (n [%])		
Female	517 [70.34%]	174 [71.90%]
Male	217 [29.52%]	68 [28.10%]
No response	1 [0.14%]	0
Age (mean ± SD) ***in years***	51.56 (± 16.64)	55.76 (± 16.07)
Education (mean ± SD)	12.22 (± 2.35)	18.16 (± 2.26)

[b] Anger measures at T2 are not analyzed in the present paper.

in years		
Race (n [%])		
White	442 [60.14%]	158 [65.29%]
White. non-Hispanic	9 [1.22%]	8 [3.31%]
Black or African American	37 [5.08%]	8 [3.31%]
American Indian or Alaska Native	3 [0.41%]	1 [0.41%]
Asian	61 [8.3%]	17 [7.02%]
Native Hawaiian or Other Pacific Islander	3 [0.41%]	2 [0.83%]
Other	89 [12.11%]	26 [10.74%]
Race and Ethnicity Unknown	1 [0.14%]	0
Patient Refused	22 [2.99%]	8 [3.31%]
Unknown	68 [9.25%]	14 [5.79%]
Ethnicity (n [%])		
Non-Hispanic/Non-Latino	590 [80.27%]	201[83.06%]
Hispanic/Latino	30 [4.08%]	18 [7.44%]
Patient Refused	18 [2.45%]	7 [2.89%]
Unknown	97 [13.2%]	16 [6.61%]
Marital status (n [%])		
Married	381 [51.84%]	119 [49.17%]
Separated	13 [1.77%]	3 [1.24%]
Widowed	32 [4.35%]	15 [6.2%]
Never married	158 [21.5%]	44 [18.18%]
Living together	50 [6.8%]	24 [9.92%]
Divorced	90 [12.24%]	35 [14.46%]
Unknown	11 [1.5%]	2 [0.83%]

Identification and description of anger profiles

Latent profile analysis procedure

LPA was run for 1-5 profile models including the anger indicator variables and assessed for model fit and clinical relevance (see Table 2). The LMR p-value changed from significant to non-significant when transitioning from the 4- to 5-profile model. Given this result, the 4-profile model and the models above and below (3- and 5-profile models) were examined for pragmatic evaluation. The 4-profile solution was preferred over the 3-profile solution because the latter failed to identify a distinct high anger and injustice group, which emerged as a potentially important clinical subgroup with 54 subjects in the 4-profile solution. The 5-profile solution had a less preferable entropy value and needlessly split the low anger and low injustice subgroup (see descriptions in the next section) into two subgroups. AIC, BIC, and

SABIC were all acceptable for the 4-profile solution. Additionally, classification probabilities for the 4-profile model indicated high assignment accuracy across groups, with diagonal probabilities ranging from 88.3% to 95.1%, further supporting its suitability (see Table S1). Hence, the 4-profile model was chosen, as it satisfied parsimony, efficiency, interpretability, and its ability to identify four discrete anger profiles.

Table 2. *Relative fit statistics for latent profile model solutions of two to five latent profiles estimated*. Abbreviations: AIC – Akaike information criteria, BIC – Bayesian information criteria, SABIC – Sample size adjusted Bayesian information criteria, LMR LRT – Lo-Mendell-Rubin likelihood ratio test. Bolded values denote that the model was selected as the most parsimonious.

	Group-Solution Models			
	2 profiles	***3 profiles***	***4 profiles***	***5 profiles***
AIC	34307	33913	**33816**	33505
BIC	34422	34070	**33816**	33744
SABIC	34343	33962	**33860**	33579
LMR LRT	1147.50, p<0.001	412.16, p=0.006	**312.86, p=0.019**	131.07, p=0.73
Entropy	0.81	0.85	**0.86**	0.83
Group size (%)	64%, 36%	59%, 21%, 20%	**49%, 20%, 7%, 24%**	7%, 42%, 24%, 20%, 7%

Characteristics of identified anger profiles

The four profiles were labeled based on their relative characteristics across all the anger-related measures (Figure 1, Table 3, and Table S2), with profiles generally differing in levels of both anger (low, medium, high) and perceived injustice (low, medium, high). Profile "LALI" (Low Anger/Low Injustice – n=359; 48.84%) was characterized by lowest levels of state-like and trait anger, lowest levels of anger expression, and highest levels of anger control. Additionally, this profile displayed the lowest scores of perceived injustice in terms of both unfairness and severity of loss. Profile "MAMI" (Medium Anger / Medium Injustice

– n=173; 23.54%) was characterized by medium levels of state-like anger, average-to-medium levels of trait anger, anger expression and anger control, and medium scores in injustice experience, again in terms of both unfairness and severity of loss. Profile "MALI" (Medium Anger/Low Injustice – n=149; 20.27%) was characterized by medium levels of state-like anger, medium-to-high levels of trait anger and anger expression, low levels of anger control, combined with below average injustice experience scores. Finally, profile "HAHI" (High Anger/High Injustice – n=54; 7.35%) was characterized by highest levels of state-like, trait anger, and anger expression, and low levels of anger control. Injustice experience scores were the highest compared to all other profiles.

Figure 1. Line graph of anger profiles with indicators standardized into z-scores and standard errors. Scores were converted to z-scores for visualization. Abbreviations: IE – Injustice experience.

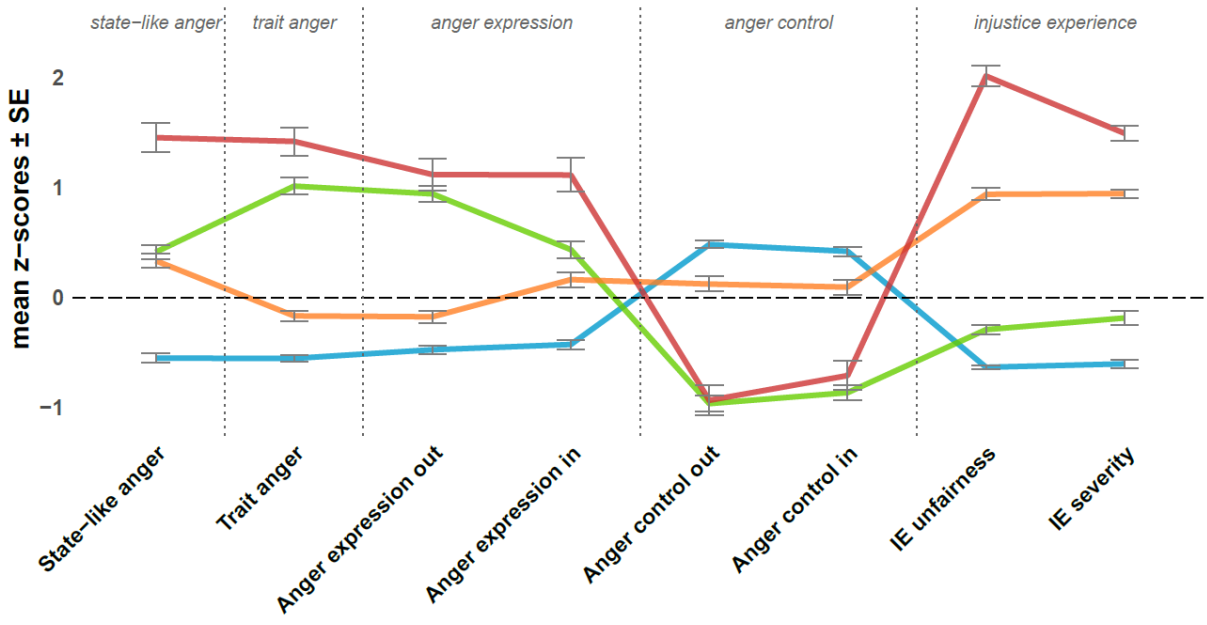

Table 3. *Descriptive and inferential statistics (ANOVA) for anger-related measures by anger profiles at baseline*. Abbreviations: IE – Injustice experience, n – number of participants, M – mean, SD – standard deviation.

Anger measures	**LALI n = 359 [M ± SD]**	**MALI n = 149 [M ± SD]**	**MAMI n = 173 [M ± SD]**	**HAHI n = 54 [M ± SD]**	**F effect**	***p* value**	**Effect size**
Sate-like anger	43.12±7.86	52.84±7.62	52.06±8.24	63.33±9.90	$F(3, 731) = 139.50$	< .001	$\eta p^2 = .364$
Trait Anger	12.60±2.35	18.87±3.71	14.15±2.39	20.50±3.78	$F(3, 731) = 255.00$	< .001	$\eta p^2 = .511$
Anger expression out	11.04±2.02	15.07±2.47	11.89±2.16	15.57±3.04	$F(3, 731) = 154.90$	< .001	$\eta p^2 = .364$
Anger expression in	13.29±3.27	16.81±3.81	15.69±3.73	19.57±4.62	$F(3, 731) = 70.53$	< .001	$\eta p2 = .224$
Anger control out	28.77±2.87	22.54±3.73	27.22±3.90	22.67±4.35	$F(3, 731) = 142.50$	< .001	$\eta p2 = .369$
Anger control in	27.65±3.72	21.66±4.02	26.14±4.26	22.39±4.55	$F(3, 731) = 93.06$	< .001	$\eta p2 = .276$
IE unfairness	1.83±2.14	3.83±3.10	11.02±4.25	17.30±4.25	$F(3, 731) = 619.50$	< .001	$\eta p2 = .718$
IE severity	7.33±4.18	9.89±5.01	16.81±3.19	20.17±3.09	$F(3, 731) = 307.10$	< .001	$\eta p2 = .558$

Results from ANOVAs confirmed significant interaction effects between profiles and every measure of anger (i.e., state-like anger, trait anger, anger expression in and out, anger control in and out, and injustice experience unfairness and loss; see Table 3). All pairwise comparisons were significantly different (corrected *p*s < .05), except for the following: MALI vs. MAMI for state-like anger ($p = .387$), and MALI vs. HAHI for anger expression out ($p = .159$), anger control out ($p = .812$), and anger control in ($p = .252$, see Table S2).

Demographic factors significantly differed across anger profiles. The LALI profile had the highest mean age (54.55 ± 16.48 years), while the HAHI profile had the youngest participants (44.77 ± 14.59 years, $p < 0.001$). Education also significantly varied ($p < 0.001$), with LALI and MALI showing the highest levels (12.45 ± 2.2 years), and HAHI the lowest (11.02 ± 3.08 years, see Table S3 for descriptive statistics of socio-demographic, clinical, and negative affect covariates by anger profile).

Effect of anger profiles on pain outcomes

Pain outcomes at baseline

Anger profiles significantly moderated outcomes across all pain assessments (*F*s > 10.74, *p*s < .001, $\eta p^2 > 0.042$; Figure 2, Table 4, and Table S4). Descriptively, the HAHI profile

reported the most severe pain outcomes, including higher pain intensity, greater pain interference, more pain behaviors, more body regions in pain, and poorer physical function in both mobility and upper body tasks. In contrast, the LALI profile demonstrated the least severe pain outcomes, with lower pain intensity, less pain interference, fewer pain behaviors, and better physical function. While the MAMI and MALI profiles were intermediates in terms of their anger-related profiling, MAMI had worse scores in all pain outcomes compared to MALI. In fact, MAMI did not differ in any of the pain outcomes from HAHI, while MALI did not differ in any of them from LALI. In other words, all pairwise comparisons were significant (ps < .05) between profiles when low injustice profiles were compared to medium or high injustice profiles (i.e., LALI vs. MAMI; LALI vs. HAHI; MALI vs. MAMI; MALI vs. HAHI; see Table S4).

Figure 2. Line graph of anger profiles across pain variables at baseline. Scores were converted to z-scores for visualization. Abbreviations: PF – Physical function.

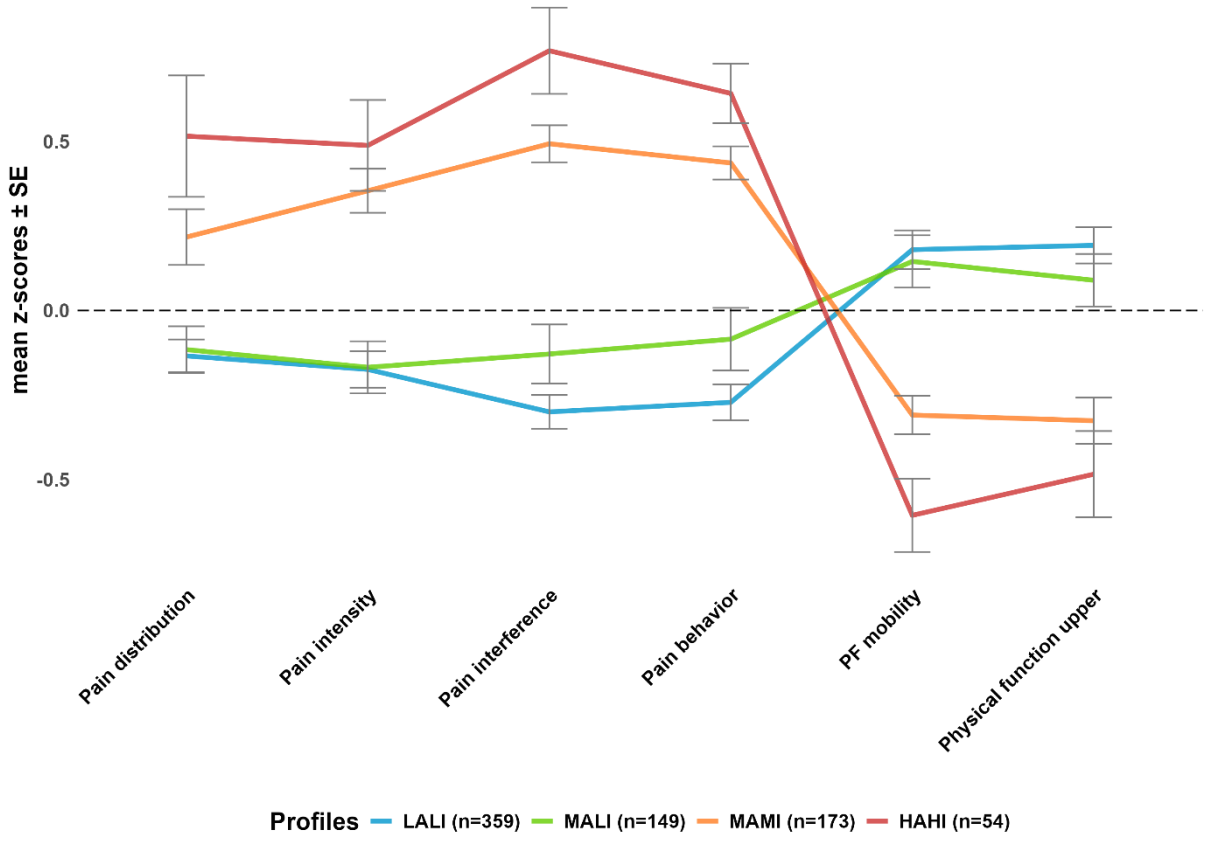

Table 4. *Descriptive and inferential statistics (ANOVA) for pain-related measures by anger profiles at baseline*. Abbreviations: PF – physical function, n – number of participants, M – mean, SD – standard deviation.

Pain measures	LALI n = 359 [M ± SD]	MALI n = 149 [M ± SD]	MAMI n = 173 [M ± SD]	HAHI n = 54 [M ± SD]	*F* effect	*p* value	Effect size
Pain distribution	11.20±12.81	11.46±11.71	16.09±15.08	20.24±18.36	$F(3, 731) = 10.74$	< .001	$\eta p^2 = 0.042$
Pain intensity	5.59±2.09	5.60±1.92	6.66±1.75	6.94±2.02	$F(3, 731) = 17.70$	< .001	$\eta p^2 = 0.068$
Pain interference	61.49±6.95	62.74±7.83	67.31±5.28	69.33±6.89	$F(3, 731) = 42.39$	< .001	$\eta p^2 = 0.148$
Pain behavior	57.23±4.78	58.10±5.33	60.57±3.05	61.54±3.06	$F(3, 731) = 31.00$	< .001	$\eta p^2 = 0.113$
PF – mobility	42.93±10.46	42.60±9.11	38.21±7.21	35.35±7.68	$F(3, 731) = 18.25$	< .001	$\eta p^2 = 0.070$
PF – upper	42.57±10.34	41.52±9.65	37.30±9.14	35.69±9.54	$F(3, 731) = 16.14$	< .001	$\eta p^2 = 0.062$

These effects remained robust even after accounting for sociodemographic (age, sex, education; Fs > 8.12, ps < .001, $\eta p^2 > 0.033$), clinical (pain duration; Fs > 8.87, ps < .001, $\eta p^2 > 0.036$), and negative affect covariates (anxiety, depression; Fs > 3.03, ps < .05, $\eta p^2 > 0.012$,

see Table 5). The only exception was the extent of pain distribution in the body, where the inclusion of negative affect covariates rendered the effect non-significant ($F = 2.02$, $p = .110$, $\eta p^2 = 0.008$). While including negative affect covariates generally reduced effect sizes, anger profiles continued to independently influence most pain-related measures.

Table 5. *Incremental ANCOVA analysis of anger profiles on pain variables at baseline*. The effects reported are for the pain variables according to the anger profiles, incrementally controlling for the covariates in the ANCOVA models. Bolded values denote significant effects.

Pain measures	Model	Covariates added	F effect	*p*-value	Effect size
Pain distribution	1	+ Sociodemographic (Age, Sex, Education)	***F*(3, 723) = 8.12**	**< .001**	$\eta p^2 = 0.033$
	2	+ Clinical (Pain duration)	***F*(3, 722) = 8.87**	**< .001**	$\eta p^2 = 0.036$
	3	+ Negative affect (Anxiety, Depression)	$F(3, 720) = 2.02$	= .110	$\eta p^2 = 0.008$
Pain intensity	1	+ Sociodemographic (Age, Sex, Education)	***F*(3, 723) = 15.67**	**< .001**	$\eta p^2 = 0.061$
	2	+ Clinical (Pain duration)	***F*(3, 722) = 15.99**	**< .001**	$\eta p^2 = 0.062$
	3	+ Negative affect (Anxiety, Depression)	***F*(3, 720) = 4.23**	**< .01**	$\eta p^2 = 0.017$
Pain interference	1	+ Sociodemographic (Age, Sex, Education)	***F*(3, 723) = 37.45**	**< .001**	$\eta p^2 = 0.134$
	2	+ Clinical (Pain duration)	***F*(3, 722) = 37.84**	**< .001**	$\eta p^2 = 0.136$
	3	+ Negative affect (Anxiety, Depression)	***F*(3, 720) = 6.18**	**< .001**	$\eta p^2 = 0.025$
Pain behavior	1	+ Sociodemographic (Age, Sex, Education)	***F*(3, 723) = 25.58**	**< .001**	$\eta p^2 = 0.096$
	2	+ Clinical (Pain duration)	***F*(3, 722) = 25.78**	**< .001**	$\eta p^2 = 0.097$
	3	+ Negative affect (Anxiety, Depression)	***F*(3, 720) = 3.29**	**< .05**	$\eta p^2 = 0.014$
Physical function - mobility	1	+ Sociodemographic (Age, Sex, Education)	***F*(3, 723) = 23.15**	**< .001**	$\eta p^2 = 0.088$
	2	+ Clinical (Pain duration)	***F*(3, 722) = 23.10**	**< .001**	$\eta p^2 = 0.088$
	3	+ Negative affect (Anxiety, Depression)	***F*(3, 720) = 6.25**	**< .001**	$\eta p^2 = 0.025$
Physical function - upper	1	+ Sociodemographic (Age, Sex, Education)	***F*(3, 723) = 18.23**	**< .001**	$\eta p^2 = 0.070$
	2	+ Clinical (Pain duration)	***F*(3, 722) = 18.26**	**< .001**	$\eta p^2 = 0.071$
	3	+ Negative affect (Anxiety, Depression)	***F*(3, 720) = 3.03**	**< .05**	$\eta p^2 = 0.012$

The average pain interference scores for both the MAMI and HAHI profiles (see Table 4) met or exceeded the clinical cutoff (PROMIS-PI T-score ≥ 65) used to define HICP[37]. The prevalence of HICP within each profile was as follows: LALI (31.8%, n = 114/359), MALI (40.9%, n = 61/149), MAMI (72.8%, n = 126/173), and HAHI (75.9%, n = 41/54). A chi-square test revealed a significant association between anger profiles and high pain interference, $\chi^2(3) = 100.23$, $p < .001$, indicating that individuals in profiles characterized by

medium-to-high levels of perceived injustice were significantly more likely to report severe pain-related disruption.

Pain outcomes at follow-up

At follow-up, anger profiles significantly predicted pain outcomes across most measures (see Table 6, Figure 3). Anger profiles moderated pain intensity, pain interference, pain behavior, and physical function tasks (Fs > 3.50, ps < .05, $\eta p^2 > 0.042$), while no significant effects were observed for pain distribution ($F = 2.60$, p = .053, $\eta p^2 = 0.032$). Post hoc pairwise comparisons revealed significant differences in pain measurements primarily between low-injustice profiles (LALI, MALI) vs. medium and high injustice profiles (MAMI, HAHI), although the pattern was less well-defined when compared to baseline. Specifically, significant differences were observed for LALI vs. MAMI, LALI vs. HAHI, and, in some cases, MALI vs. MAMI or MALI vs. HAHI (corrected ps < .05), depending on the pain measure. For instance, pain intensity showed significant differences for LALI vs. MAMI and LALI vs. HAHI, while pain interference revealed broader differences, including significant contrasts between MAMI and HAHI. However, no significant differences were found for pain distribution across all pairwise comparisons (see Table S5).

Figure 3. Line graph of anger profiles across pain variables at follow-up. Scores were converted to z-scores for visualization. Abbreviations: PF – Physical function.

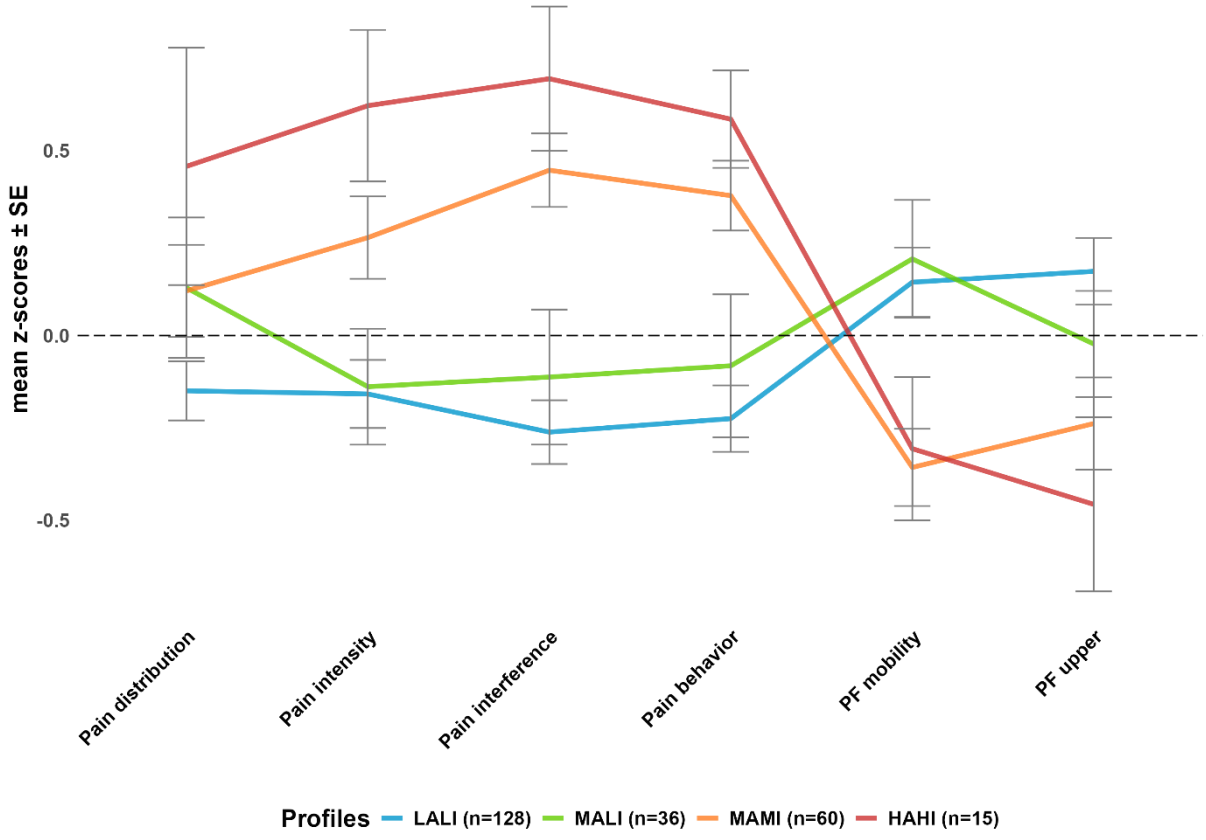

Table 6. *Descriptive and inferential statistics (ANOVA) for pain-related measures by anger profiles at follow-up.* PF = physical function. n = number of participants. M = mean. SD = standard deviation. Abbreviations: PF – physical function, n – number of participants, M – mean, SD – standard deviation.

Pain measures	LALI n = 128 [M ± SD]	MALI n = 38 [M ± SD]	MAMI n = 61 [M ± SD]	HAHI n = 15 [M ± SD]	F effect	*p*-value	Effect size
Pain distribution	10.91±12.74	14.84±16.50	14.72±13.71	19.47±17.51	$F(3, 237) = 2.60$	= .053	$\eta p^2 = 0.032$
Pain intensity	4.94±2.25	4.98±2.09	5.85±1.88	6.62±1.71	$F(3, 237) = 4.92$	< .01	$\eta p^2 = 0.059$
Pain interference	58.59±7.49	59.74±8.65	64.03±5.96	65.93±5.80	$F(3, 237) = 10.69$	< .001	$\eta p^2 = 0.119$
Pain behavior	56.45±5.20	57.18±6.10	59.54±3.78	60.60±2.61	$F(3, 237) = 7.48$	< .001	$\eta p^2 = 0.087$
PF - mobility	40.98±10.46	38.97±9.05	36.77±9.97	34.53±9.33	$F(3, 237) = 4.43$	< .01	$\eta p^2 = 0.053$
PF - upper	41.84±10.18	42.45±9.41	37.05±7.80	37.53±7.18	$F(3, 237) = 3.50$	< .05	$\eta p^2 = 0.042$

Another exploration of whether high pain interference persisted over time was tested by applying the clinical cutoff (PROMIS-PI T-score ≥ 65) to define HICP at follow-up. The rates of high pain interference across profiles were: LALI (20.3%, n = 26/128), MALI (34.2%, n = 13/38), MAMI (44.3%, n = 27/61), and HAHI (53.3%, n = 8/15). A chi-square analysis showed a significant link between anger profiles and continued high pain interference, $\chi^2(3) = 15.63$, $p < .001$, indicating that individuals with higher perceived injustice were more likely to experience ongoing pain-related disruption.

Pain outcomes over time (baseline vs. follow up)

Considering both timepoints, the effects of anger profiles were robust across all pain variables (Fs > 3.8, ps < .05, $\eta p^2 > .023$; see Table 7). In contrast, the main effects of timepoints (baseline vs. follow-up) significantly impacted only pain intensity and pain behavior, that were reduced over time (Fs > 11.3, ps < .001, ηp^2=.049). In contrast, pain distribution, pain interference, and physical function (mobility and upper body) were not significantly affected by time alone (Fs < 0.9, ps > .34, ηp^2<.002). Notably, no significant interaction effects between anger profiles and timepoints were observed (Fs < 0.94, ps > .42, ηp^2<.006), indicating that the temporal changes in pain intensity and behavior were consistent across profiles.

Table 7. *Repeated measures ANCOVA for pain variables by timepoints and anger profiles (N=242)*. Bolded values denote significant p-values.

Pain measures	Baseline (M ± SD)	Follow-up (M ± SD)	Main effect: Anger profiles	Main effect: Timepoints	Interaction: Anger profiles x Timepoints
Pain distribution	20.24 ± 18.36	19.47 ± 17.51	***F*(3, 475) = 3.81, *p* < .05, ηp^2 = .023**	$F(1, 475) = 0.88$, $p = .348$, $\eta p^2 = .002$	$F(3, 475) = 0.09$, $p = .964$, $\eta p^2 < .001$
Pain intensity	6.94 ± 2.02	6.62 ± 1.71	***F*(3, 475) = 24.51, *p* < .001, ηp^2 = .134**	***F*(1, 475) = 24.55, *p* < .001, ηp^2 = .049**	$F(3, 475) = 0.01$, $p = .997$, $\eta p^2 < .001$
Pain interference	69.33 ± 6.89	65.93 ± 6.89	***F*(3, 475) = 7.53, *p* < .001, ηp^2 = .045**	$F(1, 475) = 0.10$, $p = .756$, $\eta p^2 < .001$	$F(3, 475) = 0.19$, $p = .903$, $\eta p^2 = .001$

Pain behavior	61.54 ± 3.06	60.60 ± 2.61	***F*(3, 475) = 16.22, *p* < .001, η*p*² = .134**	***F*(1, 475) = 11.32, *p* < .001, η*p*² = .049**	*F*(3, 475) = 0.94, *p* = .422, η*p*² = .006
Physical function - mobility	35.69 ± 9.54	34.53 ± 9.33	***F*(3, 475) = 6.85, *p* < .001, η*p*² = .045**	*F*(1, 475) = 0.22, *p* = .637, η*p*² < .001	*F*(3, 475) = 0.04, *p* = .903, η*p*² < .001
Physical function - upper	35.35 ± 7.68	37.53 ± 7.18	***F*(3, 475) = 7.53, *p* < .001, η*p*² = .045**	*F*(1, 475) = 0.10, *p* = .756, η*p*² < .001	*F*(3, 475) = 0.19, *p* = .903, η*p*² = .001

General Discussion

Although anger is an adaptive emotion that enables individuals to respond to threats, to personal insults and breaches of social norms and injustices[7], it has been linked to increased symptom severity in context of CP[11,13,38]. However, much of the existing research has failed to consider the interrelationships between multiple dimensions of anger[11], potentially obscuring mechanistic and clinically relevant distinctions between various (mal)adaptive anger responses. The present study addresses this gap by using LPA to examine whether distinct anger profiles may emerge from several anger-related metrics, describing the pattern of relationships between these various anger-related metrics and illustrating the extent by which these profiles associate with pain outcomes at different timepoints. Consistent with hypotheses, four profiles were identified: Low Anger / Low Injustice (LALI), Medium Anger / Low Injustice (MALI), Medium Anger / Medium Injustice (MAMI), and High Anger / High Injustice (HAHI). These profiles demonstrated significant associations with pain measures, both at baseline and follow-up, revealing how data-driven combinations of anger dimensions, predict pain symptoms and HICP in the short and long term. Importantly, these associations persisted beyond the influence of commonly assessed emotional distress symptoms, namely anxiety and depression, supporting the unique contribution of anger to CP outcomes and their trajectories, and underscoring the need of regular assessment of anger-related metrics, especially perceived injustice, in clinical and research settings. These findings thus have important mechanistic and clinical implications.

The largest group labeled as LALI (49% of sample at baseline) was characterized by lowest anger, highest anger control, and minimal perceived injustice, and was associated with the least severe pain outcomes at baseline and follow-up, including lower pain intensity, less interference, and better physical function. This profile reflects an adaptive emotional pattern, suggesting that relatively high anger regulation may operate as a stable dispositional trait rather than solely a response to provocation or stress. This perspective is consistent with research indicating that effective anger regulation can be proactive, rather than solely reactive to threat or injustice[39]. The profile labeled MALI (20%) exhibited medium anger, reduced anger control, and low perceived injustice, with low pain outcomes, similar to those of LALI. This combination suggests that potential sources of anger in individuals within this profile may be distinct from perceptions of injustice related to their medical condition, potentially arising from non-pain-related threats, stress, frustration, or other situational factors[8]. While their anger is notable, their regulatory capacities are low, and yet this seems to be independent from their chronic pain as their pain outcomes remain relatively low. The profile labeled MAMI (24%) showed medium anger and average levels of anger expression and anger control, coupled with medium perceived injustice, resulting in more severe pain outcomes compared to LALI and MALI. This pattern underscores the amplifying effect of maladaptive cognitive processes such as perceived injustice, even in the absence of high levels of anger. Lastly, the HAHI profile (7%) combined highest levels of anger with lowest levels of anger control, and with highest levels of perceived injustice, and demonstrated the most severe pain outcomes. This profile captures a maladaptive response to chronic pain, where intense anger and high perceived injustice seem to join forces to exacerbate symptoms in the potential absence of adequate regulatory control.

Although the anger profiles reveal a descriptive pain gradient, not all dimensions of anger were equally effective in differentiating pain outcomes. Among these, perceived injustice, as

measured here by the IEQ and framed in context of patients' medical condition[25,40], emerged as particularly significant. At baseline, profiles with lower perceived injustice (i.e., LALI and MALI) consistently demonstrated better pain outcomes compared to those with medium-to-high perceived injustice (i.e., MAMI and HAHI), highlighting its pivotal role in CP[11,14,15,25,40,41]. This pattern appears to remain consistent over time, as indicated by the follow-up results. Perceived injustice reflects cognitive appraisals of unfairness, victimization, and irreparable loss that seem to exacerbate CP symptoms. These appraisals may foster further maladaptive processes such as rumination and magnification, which intensify emotional reactivity, hypervigilance, and ultimately pain interference and disability[14,25]. These mechanisms are particularly important in understanding the progression to HICP, where the interplay of cognitive and emotional factors seems to contribute to the most severe levels of disability[19,36]. Indeed, individuals with HICP[35] are characterized by the most severe functional limitations among people with CP, including marked reductions in workforce participation and elevated healthcare utilization and costs[37,42,43]. Identifying individuals at risk for HICP is crucial for effective triaging and treatment within a person-centered healthcare framework. Consistent with this, the medium-to-high injustice profiles (i.e., MAMI and HAHI) included substantially larger proportions of individuals with HICP, further emphasizing the clinical implications of the findings.

Previous findings generally align with current results, highlighting perceived injustice as a key factor in CP outcomes[44–46]. Systematic reviews and meta-analyses have shown that perceived injustice is consistently associated with worse pain intensity, greater physical disability, pain interference and overall functional impairment[15,47]. For example, a recent meta-analysis[47] reported that the prevalence of high perceived injustice ranged from 23% to 77% in CP patients, with those reporting such levels of perceived injustice exhibiting significantly higher psychological distress. Importantly, findings suggest that medium-to-high

anger, whether state or trait anger as an example, is not necessarily maladaptive, at least not in terms of measured pain outcomes; rather, it is the combination of anger with medium-to-high levels of perceived injustice that drives poorer pain outcomes. In fact, as long as one does not succumb to appraisals of injustice, having moderate levels of anger seems fine, as evident in the MALI profile. This distinction refines prior work, highlighting the need to consider the interplay of multiple anger dimensions, or by extension of emotional and cognitive factors, in understanding CP severity.

Notably, some demographic factors were unevenly distributed across profiles (see Table S3), suggesting a relationship between age and education, and anger. Participants in the LALI were older, whereas those in the HAHI profile were younger. These findings align with research indicating that older adults often demonstrate improved emotional regulation and reduced emotional reactivity compared to younger individuals, likely due to greater life experience and the development of adaptive coping strategies over time[48,49]. Education also varied across profiles, with LALI and MALI profiles showing the highest levels, while HAHI had the lowest, supporting the idea that higher education may foster emotional regulation[50]. Note that even after accounting for these socio-demographic differences, the associations between anger profiles and pain outcomes persisted (see Table 5).

In terms of exploring symptom trajectories, only pain intensity and pain behavior improved overall at follow-up, while other pain measures remained stable. These findings emphasize the coexistence of stable and dynamic components in CP: while deeply ingrained factors like pain interference and functional limitations are less responsive to short-term changes, surface-level symptoms such as pain intensity and behavior appear more amenable to potentially spontaneous reductions. Aligning with the biopsychosocial model[51,52], this complexity underscores the need for integrating immediate symptom relief strategies with deeper

interventions that target the cognitive and emotional mechanisms sustaining CP. That said, it's worth noting that these reductions were of very small effect-sizes.

Current findings offer clinically actionable insights by identifying distinct anger profiles that map onto meaningful differences in pain and disability. Higher injustice profiles (MAMI and HAHI) consistently showed the worst outcomes, positioning perceived injustice as a critical - but complex - treatment target. Yet, unlike anger[53–56], perceived injustice is notoriously resistant to change in standard multidisciplinary pain interventions, often showing the least improvement among psychosocial risk factors[25,57,58]. This likely reflects perceived injustice's deep roots in appraisals of blame, unfairness, and irreparable loss, which are difficult to directly challenge without risking invalidation. However, one evidence-supported path forward is to prioritize the formation of a strong therapeutic alliance[59]. Early empathic engagement and humanized care have been shown to reduce anger, mitigate perceived injustice, and de-escalate adversarial attitudes[60]. Results extend this by showing that disaggregating perceived injustice by co-occurring anger patterns can further guide therapeutic tailoring. For example, HAHI individuals may benefit from third-wave cognitive behavioral therapy, modules targeting forgiveness, meaning reconstruction, and emotion regulation[61], while avoiding direct invalidation of their beliefs related to injustice. In contrast, MALI individuals may respond more effectively to emotion awareness and expression therapy[62], which can help reduce maladaptive anger expression and poor affective regulation. LALI individuals, though low in both anger and perceived injustice, were not completely immune to pain burden, as they still sought treatment; however, their notable reduction in high-impact pain over time suggests a protective role of emotional regulation, supporting maintenance-level interventions like psychoeducation or self-management[63].

Several limitations warrant consideration. First, despite starting with a robust sample, the reduction to about one-third at follow-up limited the statistical power for longitudinal

analyses. This attrition not only reduced the ability to detect subtle effects over time but may also have introduced bias related to those lost to follow-up[42]. Second, although LPA was used innovatively to identify clinically meaningful anger subtypes in chronic pain and the stability of pain outcomes across profiles were examined over time, the limited sample size at follow-up prevented from conducting latent transition analysis (LTA), which generally requires larger samples (e.g., $N > 500$)[64]. The absence of LTA restricted insights into the potential fluidity or evolution of anger profiles over time. Future studies with even larger samples could incorporate LTA to better understand profile shifts and their implications for long-term pain trajectories. Third, while this study represents a significant step toward capturing the multidimensional nature of anger, it is not exhaustive. Future research should incorporate additional dimensions and assessments, both questionnaire-based[9,16] and experimental[65,66], to provide an even more comprehensive understanding of anger. Finally, the generalizability of these findings is constrained by the sample, which was drawn from patients seeking care at tertiary pain clinics within a single region (the San Francisco Bay Area). This may exclude individuals with differential pain levels or those from different socioeconomic backgrounds who are not seeking, or do not have access to, specialized medical treatment, highlighting the need for replication in more diverse and representative populations.

Conclusion

Anger is not inherently harmful - when expressed adaptively, it can serve as a motivational force, helping individuals set boundaries and navigate challenges[7,41]. Rather than eliminating anger, interventions should focus on harnessing its adaptive potential while mitigating its maladaptive processes. Achieving this balance requires a deeper understanding of how anger operates in CP, whilst considering its unique multidimensional complexity, incorporating cognitive, affective, motivational, physiological and social processes, and how these shape CP-trajectories. Findings support this perspective by demonstrating that distinct anger profiles

associate with pain outcomes cross-sectionally and predict them longitudinally, and independently so from other factors such as anxiety and depression. Perceived injustice emerged as a central factor distinguishing individuals with worse pain outcomes from those with more favorable trajectories. By characterizing these nuanced emotional patterns, this research highlights the crucial and complex role of anger in CP, contributing to the potential development of more refined, emotion-focused treatment approaches. Clinically, early identification and targeted management of high-anger patients may improve pain outcomes and reduce disability over time.

Disclosures

This work was supported in part by funding from several sources, including the Israeli Science Foundation (Grant 2127/24; GG), the Lady Davis Hebrew University Fellowship Trust (MG), and the National Institutes of Health (NIH). NIH support included grants from the National Institute on Drug Abuse (T32DA035165; SCM; K01DA053391, L30DA056944, and CTN Protocol 0149; NV) and the National Institute of Neurological Disorders and Stroke (R61NS118651, K24NS126781, K23NS104211, and R01NS128478; SCM). Additional support was provided by the Redlich Pain Endowment (SCM) and The Feldman Family Foundation Pain Research Fund (SCM and GG). We declare that we have no conflict of interest related to this study.

Data Availability

The data are available upon reasonable request from SCM. All statements in this report are solely those of the authors and do not necessarily represent the views of the National Institutes of Health (NIH).

Study Preregistration

This study hasn't been pre-registered.

Authorship Contributions

Marine Granjon: Data Curation, Formal Analysis, Writing - Original Draft, Writing - Review and Editing, Visualization. Noel Vest: Formal Analysis, Writing - Review and Editing. Sean C. Mackey: Resources, Financial Acquisition, Writing - Review and Editing. Gadi Gilam: Conceptualization, Data Curation, Formal Analysis, Writing - Review and Editing, Financial Acquisition, Supervision.

Figure Legends

Figure 1. *Line graph of anger profiles with indicators standardized into z-scores and standard errors*. Scores were converted to z-scores for visualization. Abbreviations: IE – Injustice experience.

Figure 2. *Line graph of anger profiles across pain variables at baseline*. Scores were converted to z-scores for visualization. Abbreviations: PF – Physical function.

Figure 3. *Line graph of anger profiles across pain variables at follow-up*. Scores were converted to z-scores for visualization. Abbreviations: PF – Physical function.

References

1. Cohen SP, Vase L, Hooten WM. Chronic pain: an update on burden, best practices, and new advances. *The Lancet*. 2021;397(10289):2082-2097. doi:10.1016/S0140-6736(21)00393-7

2. Gilam G, Sturgeon JA, You DS, Wasan AD, Darnall BD, Mackey SC. Negative Affect–Related Factors Have the Strongest Association with Prescription Opioid Misuse in a Cross-Sectional Cohort of Patients with Chronic Pain. *Pain Med*. 2020;21(2):e127-e138. doi:10.1093/pm/pnz249

3. Gilam G, Cramer EM, Webber KA, Ziadni MS, Kao MC, Mackey SC. Classifying chronic pain using multidimensional pain-agnostic symptom assessments and clustering analysis. *Sci Adv*. 2021;7(37):eabj0320. doi:10.1126/sciadv.abj0320

4. Landmark L, Sunde HF, Fors EA, et al. Associations between pain intensity, psychosocial factors, and pain-related disability in 4285 patients with chronic pain. *Sci Rep*. 2024;14(1):13477. doi:10.1038/s41598-024-64059-8

5. Fernandez E, Turk DC. The scope and significance of anger in the experience of chronic pain. *Pain*. 1995;61(2):165-175. doi:10.1016/0304-3959(95)00192-U

6. Okifuji A, Turk DC, Curran SL. Anger in chronic pain: Investigations of anger targets and intensity. *J Psychosom Res*. 1999;47(1):1-12. doi:10.1016/S0022-3999(99)00006-9

7. Alia-Klein N, Gan G, Gilam G, et al. The feeling of anger: From brain networks to linguistic expressions. *Neurosci Biobehav Rev*. 2020;108:480-497. doi:10.1016/j.neubiorev.2019.12.002

8. Gilam G, Hendler T. Deconstructing Anger in the Human Brain. In: Wöhr M, Krach S, eds. *Social Behavior from Rodents to Humans*. Vol 30. Current Topics in Behavioral Neurosciences. Springer International Publishing; 2015:257-273. doi:10.1007/7854_2015_408

9. Sommer I, Lukic N, Rössler W, Ettlin DA. Measuring anger in patients experiencing chronic pain - A systematic review. *J Psychosom Res*. 2019;125:109778. doi:10.1016/j.jpsychores.2019.109778

10. Spielberger CD, Sydeman SJ, Owen AE, Marsh BJ. Measuring anxiety and anger with the State-Trait Anxiety Inventory (STAI) and the State-Trait Anger Expression Inventory (STAXI). In: *The Use of Psychological Testing for Treatment Planning and Outcomes Assessment, 2nd Ed*. Lawrence Erlbaum Associates Publishers; 1999:993-1021.

11. Adachi T, Yamada K, Fujino H, Enomoto K, Shibata M. Associations between anger and chronic primary pain: a systematic review and meta-analysis. *Scand J Pain*. 2022;22(1):1-13. doi:10.1515/sjpain-2021-0154

12. Bruehl S, Burns JW, Chung OY, Chont M. Pain-related effects of trait anger expression: Neural substrates and the role of endogenous opioid mechanisms. *Neurosci Biobehav Rev*. 2009;33(3):475-491. doi:10.1016/j.neubiorev.2008.12.003

13. Galvez-Sánchez CM, Reyes del Paso GA, Duschek S, Montoro CI. The Link between Fibromyalgia Syndrome and Anger: A Systematic Review Revealing Research Gaps. *J Clin Med*. 2022;11(3):844. doi:10.3390/jcm11030844

14. Trost Z, Vangronsveld K, Linton SJ, Quartana PJ, Sullivan MJL. Cognitive dimensions of anger in chronic pain. *PAIN*. 2012;153(3):515-517. doi:10.1016/j.pain.2011.10.023

15. Carriere JS, Donayre Pimentel S, Yakobov E, Edwards RR. A Systematic Review of the Association Between Perceived Injustice and Pain-Related Outcomes in Individuals with Musculoskeletal Pain. *Pain Med*. 2020;21(7):1449-1463. doi:10.1093/pm/pnaa088

16. Fernandez E, Pham TM, Kolaparthi K, et al. Parameters of anger as related to sensory-affective components of pain. *Scand J Pain*. 2023;23(2):284-290. doi:10.1515/sjpain-2022-0131

17. Bauer J. A Primer to Latent Profile and Latent Class Analysis. In: Goller M, Kyndt E, Paloniemi S, Damşa C, eds. *Methods for Researching Professional Learning and Development: Challenges, Applications and Empirical Illustrations*. Professional and Practice-based Learning. Springer International Publishing; 2022:243-268. doi:10.1007/978-3-031-08518-5_11

18. Callahan A, Ashley E, Datta S, et al. The Stanford Medicine data science ecosystem for clinical and translational research. *JAMIA Open*. 2023;6(3):ooad054. doi:10.1093/jamiaopen/ooad054

19. Mackey S, Norris DJ, Klumpner TT. Learning Health Systems for Optimized Care and Real-World Innovative Research. *ASA Monit*. 2020;84(9):36. doi:10.1097/01.ASM.0000716916.08228.c2

20. Salmasi V, Terkawi AS, Mackey SC. Pragmatic Comparative Effectiveness Trials and Learning Health Systems in Pain Medicine. *Anesthesiol Clin*. 2023;41(2):503-517. doi:10.1016/j.anclin.2023.03.010

21. Ader DN. Developing the Patient-Reported Outcomes Measurement Information System (PROMIS). *Med Care*. 2007;45(5):S1. doi:10.1097/01.mlr.0000260537.45076.74

22. Broderick JE, DeWitt EM, Rothrock N, Crane PK, Forrest CB. Advances in Patient-Reported Outcomes: The NIH PROMIS® Measures. *EGEMS*. 2013;1(1):1015. doi:10.13063/2327-9214.1015

23. Gershon R, Rothrock NE, Hanrahan RT, Jansky LJ, Harniss M, Riley W. The development of a clinical outcomes survey research application: Assessment CenterSM. *Qual Life Res*. 2010;19(5):677-685. doi:10.1007/s11136-010-9634-4

24. Cook KF, Jensen SE, Schalet BD, et al. PROMIS measures of pain, fatigue, negative affect, physical function, and social function demonstrated clinical validity across a range of chronic conditions. *J Clin Epidemiol*. 2016;73:89-102. doi:10.1016/j.jclinepi.2015.08.038

25. Sullivan MJL, Adams H, Horan S, Maher D, Boland D, Gross R. The Role of Perceived Injustice in the Experience of Chronic Pain and Disability: Scale Development and Validation. *J Occup Rehabil*. 2008;18(3):249-261. doi:10.1007/s10926-008-9140-5

26. Scherrer KH, Ziadni MS, Kong JT, et al. Development and validation of the Collaborative Health Outcomes Information Registry body map. *Pain Rep*. 2021;6(1):e880. doi:10.1097/PR9.0000000000000880

27. Cook KF, Dunn W, Griffith JW, et al. Pain assessment using the NIH Toolbox. *Neurology*. 2013;80(11 Suppl 3):S49-53. doi:10.1212/WNL.0b013e3182872e80

28. Muthén B, Muthén L. Mplus. In: *Handbook of Item Response Theory*. Chapman and Hall/CRC; 2017.

29. Garrett ES, Zeger SL. Latent Class Model Diagnosis. *Biometrics*. 2000;56(4):1055-1067. doi:10.1111/j.0006-341X.2000.01055.x

30. Hagenaars JA, McCutcheon AL. *Applied Latent Class Analysis*. Cambridge University Press; 2002.

31. Collins LM, Lanza ST. *Latent Class and Latent Transition Analysis: With Applications in the Social, Behavioral, and Health Sciences*. John Wiley & Sons; 2009.

32. Lanza ST, Bray BC, Collins LM. An Introduction to Latent Class and Latent Transition Analysis. In: *Handbook of Psychology, Second Edition*. John Wiley & Sons, Ltd; 2012. doi:10.1002/9781118133880.hop202024

33. Lo Y, Mendell NR, Rubin DB. Testing the number of components in a normal mixture. *Biometrika*. 2001;88(3):767-778. doi:10.1093/biomet/88.3.767

34. R Core Team. R: a language and environment for statistical computing. 2018. Accessed June 21, 2024. https://www.gbif.org/tool/81287/r-a-language-and-environment-for-statistical-computing

35. Dahlhamer J. Prevalence of Chronic Pain and High-Impact Chronic Pain Among Adults — United States, 2016. *MMWR Morb Mortal Wkly Rep*. 2018;67. doi:10.15585/mmwr.mm6736a2

36. Von Korff M, DeBar LL, Krebs EE, Kerns RD, Deyo RA, Keefe FJ. Graded chronic pain scale revised: mild, bothersome, and high-impact chronic pain. *PAIN*. 2020;161(3):651. doi:10.1097/j.pain.0000000000001758

37. George SZ, Allen KD, Alvarez C, et al. Prevalence and Factors Associated With High-Impact Chronic Pain in Knee Osteoarthritis: The Johnston County Health Study. *J Pain*. 2024;25(12):104687. doi:10.1016/j.jpain.2024.104687

38. Bruehl S, Chung OY, Donahue BS, Burns JW. Anger Regulation Style, Postoperative Pain, and Relationship to the A118G Mu Opioid Receptor Gene Polymorphism: A Preliminary Study. *J Behav Med*. 2006;29(2):161-169. doi:10.1007/s10865-005-9030-7

39. Deffenbacher JL, Oetting ER, Lynch RS, Morris CD. The expression of anger and its consequences. *Behav Res Ther*. 1996;34(7):575-590. doi:10.1016/0005-7967(96)00018-6

40. Yakobov E, Scott W, Stanish W, Dunbar M, Richardson G, Sullivan M. The role of perceived injustice in the prediction of pain and function after total knee arthroplasty. *PAIN®*. 2014;155(10):2040-2046. doi:10.1016/j.pain.2014.07.007

41. Gilam G, Silvert J, Raev S, et al. Perceived Injustice and Anger in Fibromyalgia With and Without Comorbid Mental Health Conditions: A Hebrew Validation of the Injustice Experience Questionnaire. *Clin J Pain*. 2024;40(6):356. doi:10.1097/AJP.0000000000001204

42. Dettori JR. Loss to follow-up. *Evid-Based Spine-Care J*. 2011;2(1):7-10. doi:10.1055/s-0030-1267080

43. Mackey S. Future Directions for Pain Management: Lessons from the Institute of Medicine Pain Report and the National Pain Strategy. *Hand Clin*. 2016;32(1):91-98. doi:10.1016/j.hcl.2015.08.012

44. Carriere JS, Martel ,Marc-Olivier, Kao ,Ming-Chih, Sullivan ,Michael JL, and Darnall BD. Pain behavior mediates the relationship between perceived injustice and opioid prescription for chronic pain: a Collaborative Health Outcomes Information Registry study. *J Pain Res*. 2017;10:557-566. doi:10.2147/JPR.S128184

45. Carriere JS, Sturgeon JA, Yakobov E, Kao MC, Mackey SC, Darnall BD. The Impact of Perceived Injustice on Pain-related Outcomes: A Combined Model Examining the Mediating Roles of Pain Acceptance and Anger in a Chronic Pain Sample. *Clin J Pain*. 2018;34(8):739. doi:10.1097/AJP.0000000000000602

46. Sturgeon JA, Carriere JS, Kao MCJ, Rico T, Darnall BD, Mackey SC. Social Disruption Mediates the Relationship Between Perceived Injustice and Anger in Chronic Pain: a Collaborative Health Outcomes Information Registry Study. *Ann Behav Med*. 2016;50(6):802-812. doi:10.1007/s12160-016-9808-6

47. Roose E, Lahousse A, Robbeets A, et al. The Prevalence of Perceived Injustice and Factors Associated With Perceived Injustice in People With Pain: A Systematic Review With Meta-analysis. *Pain Physician*. 2023;26(2):E1-E49.

48. Carstensen LL, Fung HH, Charles ST. Socioemotional Selectivity Theory and the Regulation of Emotion in the Second Half of Life. *Motiv Emot*. 2003;27(2):103-123. doi:10.1023/A:1024569803230

49. Scott SB, Sliwinski MJ, Blanchard-Fields F. Age differences in emotional responses to daily stress: The role of timing, severity, and global perceived stress. *Psychol Aging*. 2013;28(4):1076-1087. doi:10.1037/a0034000

50. Gross JJ, John OP. Individual differences in two emotion regulation processes: Implications for affect, relationships, and well-being. *J Pers Soc Psychol*. 2003;85(2):348-362. doi:10.1037/0022-3514.85.2.348

51. Gatchel RJ, Peng YB, Peters ML, Fuchs PN, Turk DC. The biopsychosocial approach to chronic pain: Scientific advances and future directions. *Psychol Bull*. 2007;133:581-624. doi:10.1037/0033-2909.133.4.581

52. Nicholas MK. The biopsychosocial model of pain 40 years on: time for a reappraisal? *PAIN*. 2022;163(S1):S3. doi:10.1097/j.pain.0000000000002654

53. Bjureberg J, Ojala O, Berg A, et al. Targeting maladaptive anger with brief therapist-supported internet-delivered emotion regulation treatments: A randomized controlled trial. *J Consult Clin Psychol*. 2023;91(5):254-266. doi:10.1037/ccp0000769

54. Fernandez E. Toward an Integrative Psychotherapy for Maladaptive Anger. In: Potegal M, Stemmler G, Spielberger C, eds. *International Handbook of Anger: Constituent and Concomitant Biological, Psychological, and Social Processes*. Springer; 2010:499-513. doi:10.1007/978-0-387-89676-2_28

55. Lee AH, DiGiuseppe R. Anger and aggression treatments: a review of meta-analyses. *Curr Opin Psychol*. 2018;19:65-74. doi:10.1016/j.copsyc.2017.04.004

56. Slavin-Spenny O, Lumley MA, Thakur ER, Nevedal DC, Hijazi AM. Effects of Anger Awareness and Expression Training versus Relaxation Training on Headaches: A Randomized Trial. *Ann Behav Med*. 2013;46(2):181-192. doi:10.1007/s12160-013-9500-z

57. Yakobov E, Scott W, Stanish WD, et al. Reductions in Perceived Injustice are Associated With Reductions in Disability and Depressive Symptoms After Total Knee Arthroplasty. *Clin J Pain*. 2018;34(5):415. doi:10.1097/AJP.0000000000000551

58. Trost Z, Sturgeon J, Agtarap S, et al. The impact of perceived injustice on pain and psychological outcomes after traumatic injury: a longitudinal analysis. *Pain*. 2024;165(7):1583-1591. doi:10.1097/j.pain.0000000000003160

59. Grant-Freemantle MC, Moore J, McBrien D, Condon F, Harmon DC. The role of perceived patient injustice on pain related and functional outcomes in orthopaedic patients; a systematic review. *J Orthop*. 2023;36:19-23. doi:10.1016/j.jor.2022.12.006

60. Phelps G, Dalton S. Demonstrable professionalism: linking patient-centred care and revalidation. *Intern Med J*. 2013;43(11):1254-1256. doi:10.1111/imj.12280

61. McCracken LM, Yu L, Vowles KE. New generation psychological treatments in chronic pain. *BMJ*. 2022;376:e057212. doi:10.1136/bmj-2021-057212

62. Lumley MA, Schubiner H. Emotional Awareness and Expression Therapy for Chronic Pain: Rationale, Principles and Techniques, Evidence, and Critical Review. *Curr Rheumatol Rep*. 2019;21(7):30. doi:10.1007/s11926-019-0829-6

63. Vowles KE, McCracken LM, O'Brien JZ. Acceptance and values-based action in chronic pain: A three-year follow-up analysis of treatment effectiveness and process. *Behav Res Ther*. 2011;49(11):748-755. doi:10.1016/j.brat.2011.08.002

64. Nylund-Gibson K, Garber AC, Carter DB, et al. Ten frequently asked questions about latent transition analysis. *Psychol Methods*. 2023;28(2):284-300. doi:10.1037/met0000486

65. Gilam G, Abend R, Shani H, Ben-Zion Z, Hendler T. The anger-infused Ultimatum Game: A reliable and valid paradigm to induce and assess anger. *Emotion*. 2019;19(1):84-96. doi:10.1037/emo0000435

66. Lobbestael J, Arntz A, Wiers RW. How to push someone's buttons: A comparison of four anger-induction methods. *Cogn Emot*. 2008;22(2):353-373. doi:10.1080/02699930701438285