Sensitivity to ambient temperature increases in fibromyalgia and CRPS

Dear Editor,

People with chronic pain often report that their symptoms are exacerbated by weather conditions, such as cold ambient temperature. Some studies find that sensitivity to ambient temperature is reported more frequently by people with fibromyalgia than other pain conditions (1), although others find no such evidence (2). In our experience, people with CRPS can also report weather and temperature sensitivities. However, research on this topic is scarce, and it is not clear if the nature of their reports is different to that of people with fibromyalgia or other pain conditions. Although previous studies mainly examined exacerbation of pain by weather, we have noticed that people with pain conditions often prefer broader terms when describing these effects, such as discomfort or distress. Furthermore, our impression has been that people with CRPS or fibromyalgia sometimes indicate with curious specificity the temperatures at which they feel their symptoms are exacerbated.

To evaluate whether there is any empirical support for our above observations, we recently collected data on sensitivity to ambient temperature as part of a broader online survey on bodily changes and environmental triggers. We distributed the link to people who had previously taken part in our research; a community participant panel; patient charities; newsletters; via social media; and through friends and relatives. We received 2200 responses, of which 1501 (68.23%) were included. Exclusion was based on age ≤16 years (*N*=13), missing data (*N*=666), inconsistent answers (*N*=6) and double entries (*N*=14). Respondents were allocated to one of five groups based on whether they reported to experience pain on

most days for ≥3 months, and their declared diagnoses or lack thereof: CRPS (*N*=339), fibromyalgia (*N*=409), both CRPS and fibromyalgia ("CRPS+fibromyalgia"; *N*=79), pain controls (*N*=280), and pain-free controls (*N*= 394; Supplementary Table 1). Regarding the questions about ambient temperature, respondents were asked in separate questions if "cold weather" or "warm/hot weather" gave them pain, discomfort, or distress ("pain/discomfort/distress triggers"; see Appendix). Respondents in the pain groups were additionally asked if "cold weather" or "warm/hot weather" made their pain worse ("pain intensifier"). We compared groups regarding the proportions of respondents who reported sensitivity to cold or warm/hot weather with Chi square tests (using Bonferroni correction for post-hoc comparisons).

Overall, a higher proportion of people with CRPS and/or fibromyalgia reported cold or warm/hot weather as intensifying their pain; and triggering pain, discomfort, and distress compared to pain(-free) controls (Figure 1). Among the CRPS and fibromyalgia groups, there were no differences between the proportions of people with CRPS, fibromyalgia, and CRPS+fibromyalgia who reported that cold weather intensified pain; or triggered pain, discomfort, or distress. However, differences between these three groups emerged with regard to warm/hot weather. People with CRPS (with or without fibromyalgia) reported more often that warm/hot weather *intensifies* and *triggers pain* than people with fibromyalgia only. People with fibromyalgia reported more often that warm/hot weather *triggers discomfort* than people with CRPS.

Results were largely the same when corrected for several covariates (Supplementary Table 3 and 4). Depression, anxiety, pain duration in years, hours of pain per day, number of pain-related diagnoses, and gender were additional predictors for weather sensitivity. It should be

noted that a dissociation can be made between ‘warm’ and ‘cold’ CRPS, with a higher contribution of inflammatory mechanisms to the warm sub-type (3). Potentially, weather sensitivity differs between these sub-types. Future research is needed to study potential differences between sub-types more thoroughly.

Those respondents who indicated that cold or warm/hot weather intensifies their pain; or triggers pain, discomfort, or distress, were invited to enter into free-text boxes the specific temperatures at which they begin to feel these effects. Compared to pain(-free) controls, respondents with CRPS and/or fibromyalgia more often provided temperatures as intensifying pain; or triggering pain, discomfort, and distress (Figure 2). This group difference persisted when we considered only respondents who provided non-integer temperatures.

We used ANOVAs to compare the average temperature thresholds between groups (using Bonferroni correction for post-hoc comparisons). The lower and upper temperature thresholds that were reported to *intensify* pain did not differ between groups (Figure 3). Similarly, all groups reported similar *lower* temperatures that would trigger pain, discomfort, or distress. However, the thresholds for *warm/hot* weather to trigger pain, discomfort or distress was lower for people with CRPS or fibromyalgia compared to pain-free controls. It should be noted that we only collected temperature data of people who selected cold or warm/hot weather as pain intensifier or pain/discomfort/distress trigger, *and* who reported a specific temperature, which lead to a selection bias of weather-sensitive people who were able to report a specific temperature (see previous paragraph). This could explain why groups did not differ regarding the lower temperature thresholds.

Our survey included an additional question in which respondents could list, in free-text boxes, any additional pain intensifier or pain/discomfort/distress trigger that we had not pre specified. Slightly more people with CRPS and/or fibromyalgia reported other weather-related intensifiers/triggers than pain(-free) controls (CRPS+fibromyalgia: 1.3%/3.8%; CRPS: 5.6%/5.9%; fibromyalgia: 3.2%/3.2%, pain controls: 2.9%/2.9%, pain-free controls: 0). These regarded mainly humidity, (changes in) barometric pressure, and (thunder)storms.

Our results confirm our suspicion that people with CRPS report exacerbation of their symptoms by ambient temperature to a broadly comparable extent as people with fibromyalgia, and to a greater extent than people with other pain conditions. Furthermore, as far as we are aware, ours is the first attempt to differentiate between different effects of ambient temperature (i.e. intensifying pain or triggering pain/discomfort/distress) on people with CRPS and/or fibromyalgia compared to pain(-free) controls. People with CRPS reported more often that warm/hot weather intensified or triggered *pain*, whereas more people with fibromyalgia reported that warm/hot weather triggered *discomfort*. These results show that differentiating between *pain*, *discomfort*, and *distress* is useful as, most likely; they all negatively affect quality of life. These categories seem therefore important to include in future studies.

Previous studies looking into correlations between day-to-day temperature recordings and symptoms have found no, or very limited, statistically significant relationships between fibromyalgic pain and temperature (2). In lab settings, however, both people with CRPS and fibromyalgia are more sensitive to cold and hot stimulation compared to people with other types of pain (4). This discrepancy might be explained by heterogeneous populations with respect to temperature sensitivity and difference between outside and indoor temperatures. A

recent, large study of people with mainly arthritic conditions found that humidity, barometric pressure, and wind speed on a given day predicted pain, but not temperature or precipitation (5). This highlights potential discrepancies between true effects of weather on pain, and patients' subjective impressions. Future research is needed to investigate actual versus perceived effects of weather on pain.

In conclusion, respondents with CRPS and/or fibromyalgia reported being more sensitive to both cold and warm/hot ambient temperatures compared to pain(-free) controls. These findings emphasize the importance of considering beliefs on temperature sensitivity in CRPS and fibromyalgia to identify weather-sensitive people with CRPS or fibromyalgia, so that they can be made aware of how temperature might affect them and prepare strategies to cope with, for example, cold or hot environments.

Dr Antonia F. Ten Brink

Department of Psychology and Centre for Pain Research, University of Bath, Bath, UK

t.ten.brink@bath.ac.uk

Dr Andreas Goebel

Pain Research Institute, University of Liverpool, Liverpool, UK, and Walton Centre NHS Foundation Trust, Liverpool, UK

Dr Richard Berwick

Pain Research Institute, University of Liverpool, Liverpool, UK, and Walton Centre NHS Foundation Trust, Liverpool, UK

Prof Dr Candida S. McCabe

Royal United Hospitals NHS Foundation Trust, Bath, UK; University of the West of England, Bristol, UK; and The Florence Nightingale Foundation, London, UK

Dr Janet H. Bultitude

Department of Psychology and Centre for Pain Research, University of Bath, Bath, UK

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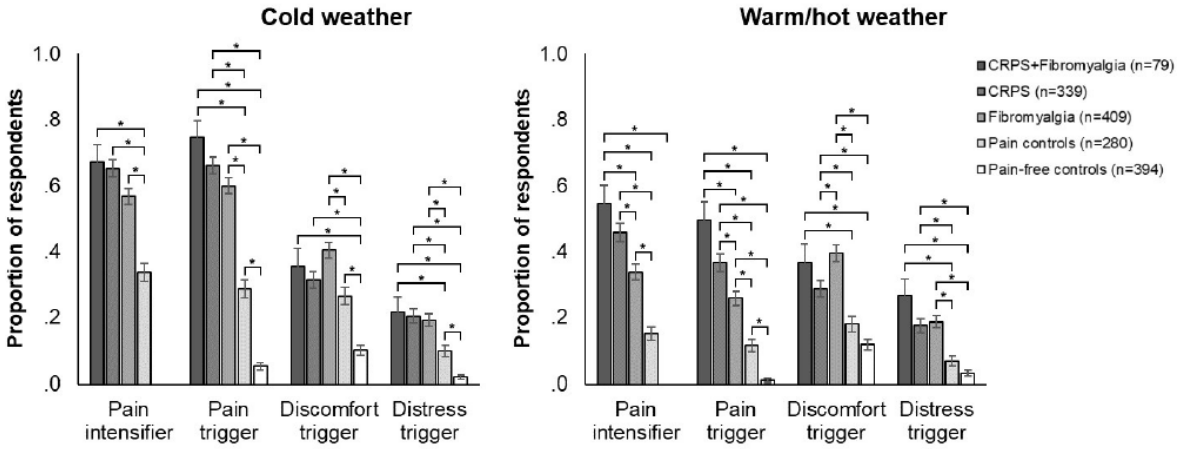

Figure 1. The proportion of respondents selecting cold (left panel) or warm/hot weather (right panel) as a pain intensifier or pain/discomfort/distress trigger. Error bars indicate one standard error of the mean.

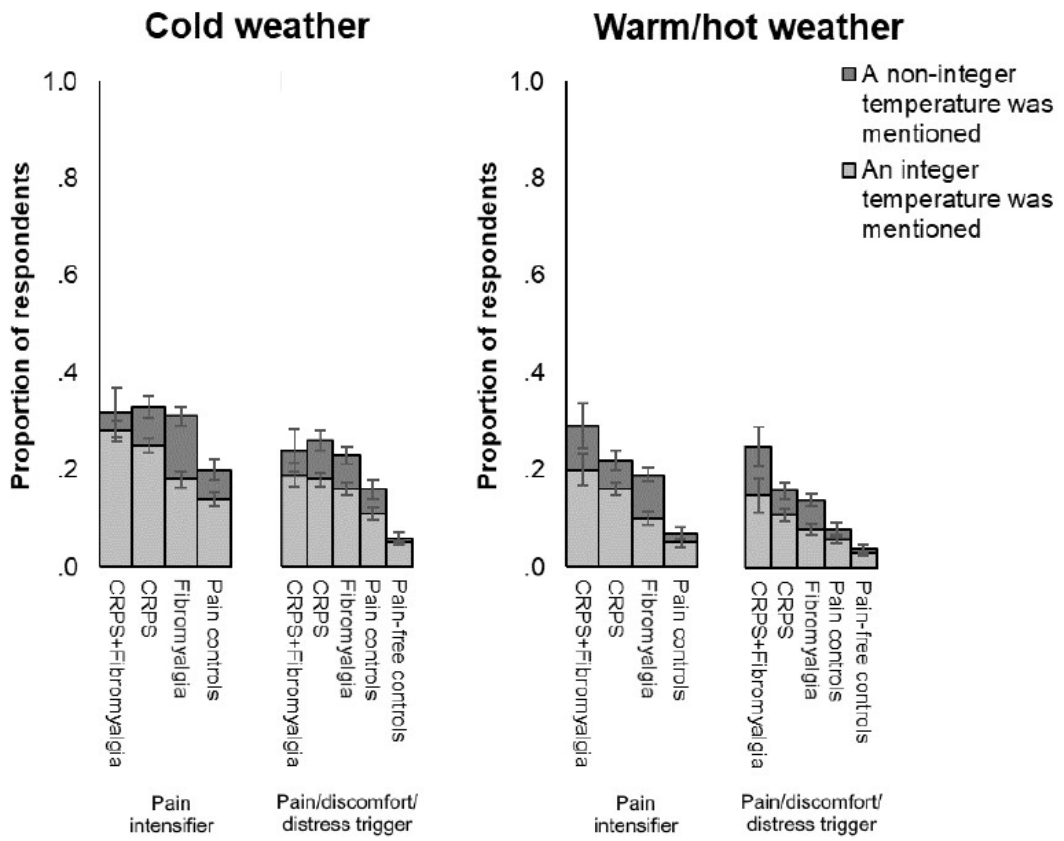

Figure 2. The proportion of respondents providing a cold (left panel) or warm/hot (right panel) temperature as a pain intensifier or pain/discomfort/distress trigger, split for respondents providing an integer versus non-integer. Error bars indicate one standard error of the mean.

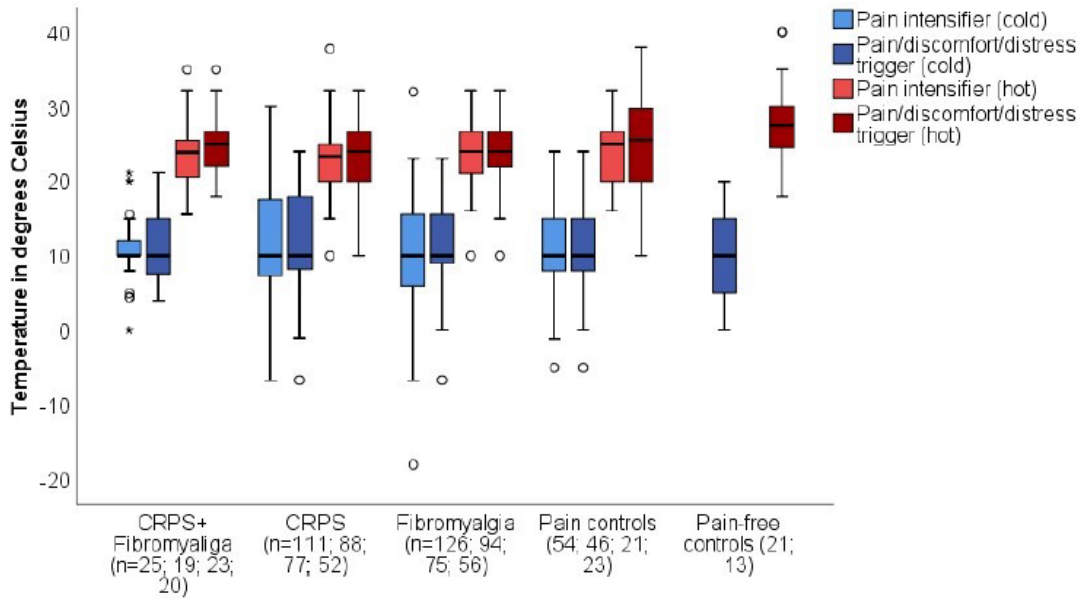

Figure 3. The temperatures (in degrees Celsius) that were reported to intensify pain or trigger pain/discomfort/distress. Note that the number of respondents differs per variable and group, as not everyone reported a temperature for each question (see Figure 2). Error bars indicate 95% confidence intervals.

Appendix

Supplementary Table 1. Demographics, depression, anxiety, and pain-related characteristics, means (SD) and percentages, split per group.

	N	CRPS	*N*	Fibromyalgia	*N*	CRPS+ Fibromyalgia	*N*	Pain controls	*N*	Pain-free controls	Statistics
Age, in years	339	46.50 (12.41)[4,5]	409	46.74 (12.08)[4,5]	79	46.01 (11.16)[4,5]	280	41.96 (16.79)[1,2,3,5]	394	34.62 (16.40)[1,2,3,4]	$F(4) = 46.84$, $p < .001$
Gender[a]	339		409		79		280		394		$\chi^2(4) = 97.55$, $p < .001$
- Female		300 (88.5%)[2,5]		380 (92.9%)[1,4,5]		75 (94.9%)[4,5]		224 (80.0%)[2,3,4]		285 (72.3%)[1,2,3,4]	
- Male		39 (11.5%)		23 (5.6%)		4 (5.1%)		51 (18.2%)		108 (27.4%)	
- Other		0		6 (1.5%)		0		5 (1.8%)		1 (0.3%)	
Depression (PHQ-9; 0-27)	314	15.62 (6.52)[4,5]	362	16.33 (6.06)[4,5]	70	16.73 (6.26)[4,5]	259	10.84 (7.00)[1,2,3,5]	387	5.99 (4.90)[1,2,3,4]	$F(4) = 180.94$, $p < .001$
Anxiety (GAD-7; 0-21)	314	10.66 (6.06)[4,5]	362	11.01 (5.86)[4,5]	70	11.09 (5.95)[4,5]	259	7.90 (5.99)[1,2,3,5]	387	4.93 (4.58)[1,2,3,4]	$F(4) = 73.03$, $p < .001$
Pain duration in years	337	8.79 (8.17)[2,3]	409	13.48 (10.75)[1,4]	78	12.35 (10.05)[1]	279	10.03 (10.74)[2]	-	-	$F(3) = 15.26$, $p < .001$
Hours of pain per day	339	18.38 (6.90)[2,4]	409	16.25 (7.19)[1,3,4]	79	19.75 (6.19)[2,4]	280	10.33 (8.06)[1,2,3]	-	-	$F(3) = 75.07$, $p < .001$
Number of pain-related medical diagnoses	339	2.12 (1.57)[2,3,4]	409	3.56 (2.04)[1,3,4]	79	4.85 (2.41)[1,2,4]	280	1.67 (1.76)[1,2,3]	-	-	$F(3) = 103.11$, $p < .001$
Pain intensity in the past week (0-10)	339	6.62 (2.14)[2,3,4]	409	7.05 (1.54)[1,4]	79	7.42 (1.61)[1,4]	280	5.11 (2.27)[1,2,3]	-	-	$F(3) = 67.17$, $p < .001$

Abbreviations: GAD-7, Generalized Anxiety Disorder-7; PHQ-9, Patient Health Questionnaire-9.

Note. The number of respondents differ per variable, as some respondents closed the survey before finishing it and only answers provided to that point were included.

[a]We did not include the 'other' group in the statistical comparison of gender, as the expected counts would be less than 5 in some cells.

We used one-way ANOVA's and a Chi-square test to compare the groups. We used the Holm-Bonferroni method to correct for multiple comparisons for the post-hoc tests.

Group mean differed significantly from [1]CRPS, [2]fibromyalgia, [3]CRPS+fibromyalgia, [4]pain controls, and [5]pain-free controls.

Supplementary Table 2. Logistic regression results predicting sensitivity for **cold weather**, including respondents with CRPS, fibromyalgia and pain controls (*N*=921).

	Pain intensifier			**Pain trigger**			**Discomfort trigger**			**Distress trigger**		
	B	SE	OR	B	SE	OR	B	SE	OR	B	SE	OR
Intercept	-1.220	.327		-1.113	.335		-1.76	.348		-4.233	.518	
Age	-0.002	.005	1.00	-0.019	.006	0.98*	-0.002	.006	1.00	0.005	.008	1.01
Depression (PHQ-9)	0.039	.018	1.04*	0.017	.018	1.02	0.011	.019	1.01	-0.002	.024	1.00
Anxiety (GAD-7)	-0.019	.018	0.98	0.020	.019	1.02	0.026	.019	1.03	0.095	.025	1.10**
Pain duration in years	0.026	.008	1.03*	0.017	.008	1.02*	0.019	.008	1.02*	0.019	.010	1.02*
Hours of pain per day	0.013	.010	1.01	0.019	.011	1.02	0.018	.011	1.02	0.032	.015	1.03*
Pain-related diagnoses	-0.005	.041	1.00	0.041	.043	1.04	0.058	.042	1.06	0.100	.051	1.11*
Pain intensity	0.014	.041	1.01	0.055	.043	1.06	-0.001	.044	1.00	0.030	.059	1.03
Gender = male (vs female)[a]	-0.401	.226	0.67	-0.590	.236	0.56*	-0.276	.245	0.76	-0.653	.361	0.52
Group = CRPS (vs pain-control)	1.048	.201	2.85**	1.309	.208	3.70**	-0.055	.215	0.95	0.333	.296	1.40
Group = fibromyalgia (vs pain-control)	0.610	.198	1.84*	0.914	.205	2.49**	0.203	.209	1.23	0.138	.292	1.15
Nagelkerke R^2	11.7%			18.7%			6.4%			14.2%		

Abbreviations: GAD-7, Generalized Anxiety Disorder-7; OR, adjusted odds ratio; PHQ-9, Patient Health Questionnaire-9; SE, standard error.

[a]We did not include the 'other' group gender, as there were not enough cases for this category.

Asterisks indicate statistical significance with alpha < .05*, and with alpha < .001**. An adjusted odds ratio of >1.0 indicates that (for every one-unit increase in the continuous variable), the risk of weather sensitivity being reported increases that many more times versus it not being reported.

Supplementary Table 3. Logistic regression results predicting sensitivity for **warm/hot weather**, including respondents with CRPS, fibromyalgia and pain controls (*N*=921).

	Pain intensifier			**Pain trigger**			**Discomfort trigger**			**Distress trigger**		
	B	SE	OR	B	SE	OR	B	SE	OR	B	SE	OR
Intercept	-3.517	0.418		-3.469	0.443		-2.197	0.382		-4.525	0.568	
Age	0.014	0.006	1.01*	-0.001	0.007	1.00	-0.004	0.006	1.00	0.006	0.008	1.01
Depression (PHQ-9)	0.023	0.019	1.02	0.037	0.021	1.04	-0.021	0.020	0.98	0.021	0.025	1.02
Anxiety (GAD-7)	-0.004	0.020	1.00	-0.007	0.021	0.99	0.057	0.020	1.06*	0.052	0.026	1.05*
Pain duration in years	0.013	0.008	1.01	0.004	0.009	1.00	0.003	0.008	1.00	0.016	0.010	1.02
Hours of pain per day	0.047	0.012	1.05**	0.045	0.013	1.05**	0.035	0.012	1.04*	0.040	0.016	1.04*
Pain-related diagnoses	0.105	0.044	1.11*	0.067	0.045	1.07	0.138	0.044	1.15*	0.107	0.052	1.11*
Pain intensity	0.014	0.046	1.01	0.084	0.050	1.09	-0.017	0.047	0.98	0.009	0.062	1.01
Gender = male (vs female)[a]	-0.379	0.261	0.68	-0.681	0.302	0.51*	-0.781	0.300	0.46*	-1.520	0.530	0.22*
Group = CRPS (vs pain-control)	1.164	0.233	3.20**	0.902	0.253	2.46**	0.365	0.238	1.44	0.647	0.335	1.91
Group = fibromyalgia (vs pain-control)	0.426	0.239	1.53	0.188	0.262	1.21	0.664	0.231	1.94*	0.475	0.332	1.61
Nagelkerke R^2	17.7%			15.6%			12.1%			15.0%		

Abbreviations: GAD-7, Generalized Anxiety Disorder-7; OR, adjusted odds ratio; PHQ-9, Patient Health Questionnaire-9; SE, standard error.

[a]We did not include the 'other' group gender, as there were not enough respondents in this category.

Asterisks indicate statistical significance with alpha < .05*, and with alpha < .001**. An adjusted odds ratio of >1.0 indicates that (for every one-unit increase in the continuous variable), the risk of weather sensitivity being reported increases that many more times versus it not being reported.

Survey questions

Below you can find the survey questions that we used for the current study.

What is your age in years?

▼ Under 16 ... 100 or older

What is your gender?

▼ Male, Female, Other

Have you been experiencing pain on most days for three months or more?

- ○ YES
- ○ NO

On average, for how many **hours** per day do you normally feel pain? Please answer using **numbers**. For example, half an hour would be ".5", and two hours would be "2".

- ○ Hours per day _____

For approximately how long have you been experiencing pain? Please answer in **years** and **months**. For example, 6 months would be “0" years and "6" months.

- ○ Years _____
- ○ Months _____

Please rate your average level of pain that you have experienced in your body OVERALL over the last week (that is, averaged across all your painful body parts).

	No pain									Worst pain imagineable
	0	1	2	3	4	5	6	7	8	9	10
Overall pain											

Have you received a medical diagnosis for your pain condition? Here, a medical diagnosis is a diagnosis that has been determined by a medical practitioner such as a GP, specialist doctor (e.g. rheumatologist or pain specialist), physiotherapist, occupational therapist, or nurse.

- ○ YES
- ○ NO

Please select all medical diagnoses that you have received for your pain condition.

- ○ Complex Regional Pain Syndrome (also known as Reflex Sympathetic Dystrophy, Causalgia, or Sudeck's syndrome)
- ○ Rheumatoid Arthritis
- ○ Osteoarthritis
- ○ Plantar fasciitis
- ○ Fibromyalgia
- ○ Hypermobility
- ○ Back pain
- ○ Migraine
- ○ Cluster Headache
- ○ Multiple Sclerosis
- ○ Neuralgia
- ○ Stomach ulcer
- ○ Endometriosis
- ○ Irritable Bowel Disease
- ○ Crohn's Disease
- ○ Other (Please specify. You can specify more than one thing if you wish)_____
- ○ I have not received any diagnosis for my pain condition

Do any of the following give you pain? Please select ANY that apply.
Do any of the following give you discomfort? Please select ANY that apply.
Do any of the following give you distress? Please select ANY that apply.
Do any of the following make your pain worse? Please select ANY that apply.

The list of items below was used for each of the previous four questions. The items that were used for the current study are depicted in bold; the other items were being analyzed as part of a wider study.

- ○ Caffeine
- ○ Alcohol
- ○ Bright lights
- ○ Flashing lights
- ○ High-contrast images, such as black and white stripes spaced close together
- ○ Loud or unpleasant noises
- ○ The touch of clothing/water/breeze
- ○ Particular foods. If yes, please specify _____
- ○ Particular smells. If yes, please specify _____
- ○ **Cold weather. if yes, then please specify from what temperature your pain starts_____**
- ○ **Warm or hot weather. If yes, then please specify from what temperature your pain starts _____**
- ○ **Other (Please specify. You can specify more than one thing if you wish)_____**

Patient Health Questionnaire (PHQ-9)

Over the last 2 weeks, how often have you been bothered by any of the following problems?

	Not at all	Several days	More than half days	Nearly every day
Little interest or pleasure in doing things	○	○	○	○
Feeling down, depressed, or hopeless	○	○	○	○
Trouble falling/staying asleep, sleeping too much	○	○	○	○
Feeling tired or having little energy	○	○	○	○
Poor appetite or overeating	○	○	○	○
Feeling bad about yourself – or that you are a failure or have let yourself or your family down	○	○	○	○
Trouble concentrating on things, such as reading the newspaper or watching television	○	○	○	○
Moving or speaking so slowly that other people could have noticed	○	○	○	○
Or the opposite – being so fidgety or restless that you have been moving around a lot more than usual	○	○	○	○
Thoughts that you would be better off dead or of hurting yourself in some way	○	○	○	○

Generalized Anxiety Disorder (GAD-7)

Over the last 2 weeks, how often have you been bothered by any of the following problems?

	Not at all	Several days	More than half days	Nearly every day
Feeling nervous, anxious, or on edge	○	○	○	○
Not being able to stop or control worrying	○	○	○	○
Worrying too much about different things	○	○	○	○
Trouble relaxing	○	○	○	○
Being so restless that it's hard to sit still	○	○	○	○
Becoming easily annoyed or irritable	○	○	○	○
Feeling afraid as if something awful might happen	○	○	○	○