Title

Quantifying intra-individual variability in anatomical sites of pain in longitudinal studies

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Data availability

Data analysis script code is available on Open Science Framework. Requests to access data should be addressed to the corresponding author and will be reviewed using the criteria specified at Madden, Msolo [15].

Abstract

Longitudinal pain studies present an opportunity to understand intra-individual variations in pain. However, current methods to quantify the anatomical extent of pain fail to capture variations across multiple body sites over time. Our aims were to (1) describe patterns of intra-individual variation in pain sites over time, (2) develop a metric that quantifies intra-individual variation in pain sites over time, and (3) determine whether this metric is related to other indicators of pain burden. We used data from a longitudinal cohort of 72 participants (51 female; median (IQR) age 43 (37-51) years) living with virally suppressed HIV, who provided weekly reports of pain severity, pain site(s), and distress over 49 weeks. Participant reports showed noteworthy intra-individual changes in pain sites over time. The pain sites variation metric, based on 727 consecutive reports from 53 participants, reflected intra-individual temporal variation in pain sites, and distinguished participants with consistent pain sites from participants with high temporal variation in pain sites. The metric was positively associated with pain severity and emotional distress, but only when unadjusted for the count of painful sites. Thus, using a longitudinal cohort, we developed a metric that quantifies individual temporal variability in pain sites and demonstrated its relationship to two frequently used metrics of pain burden, namely pain severity and distress. This metric provides an opportunity to study whether the number of, and variability in, pain sites contributes to pain burden and clinical outcomes.

Key words

pain; pain measurement; data visualisation; HIV; psychological distress

Introduction

Repeated measurements of pain reveal high levels of intra-individual variability, whether they are measured in the short term (e.g., during a quantitative sensory testing session) or the long term (e.g., longitudinal clinical trials) [14, 17]. While methods for dealing with temporal variability in pain *severity* ratings exist and range from simple (e.g., averaging over repeated measurements [22]) to sophisticated (e.g., calculating indices that incorporate the variability [17]), finding suitable methods to represent intra-individual variation in pain *sites* across time remains a challenge.

Recent data from a 48-week study of pain in people living with HIV indicated that, even when a person reports pain consistently over time, the site of that pain may vary considerably [28]. This variation in pain sites highlights the importance of recording the site(s) of pain in long-term studies, to avoid misinterpreting pain that is repeatedly reported over a prolonged period as persistent pain when it may indicate short-lived pains in multiple sites with temporal overlap.

In cross-sectional studies, pain sites are typically quantified using simple counts. In longitudinal studies, these methods are inadequate and conceal intra-individual variation over time. What is needed is a metric of the temporal variation in pain sites. Tracking absolute pain site counts at each sampling interval, or changes in the count of endorsed sites [e.g. 6] , is inadequate. For example, in a person who reports pain in their head in week 1, and pain in their hip, ankle, and shoulder (but not their head) in week 2, the pain count has gone from 1 site to 3 sites, a change of 2 sites—but the person has actually reported 4 changes in pain sites because a negative change (loss of the head as a pain site) may be as relevant as a positive change (gain of hip, ankle, and shoulder as pain sites). A metric of temporal variations in body site endorsement must capture changes in site, regardless of the direction of change.

Here, we report our approach to describing and quantifying variability in weekly measurements of pain sites in a cohort of people living with well-controlled HIV. This cohort formed part of a primary

study investigating the effect of psychological distress on pain in people living with HIV [15]. We consider this cohort ideal for studying pain site variation because people living with HIV have previously been found to have high variation in pain sites [28]. The current dataset provides fine-grained data on week-to-week fluctuations in sites and severity of pain. In addition to describing patterns of intra-individual variation in pain sites and developing a metric that quantifies that variation, a secondary objective was to determine whether our pain sites variation metric was positively associated with the within-participant mean count of painful sites, pain severity, or variance in pain severity, or emotional distress.

Methods

Study overview

This longitudinal, observational study entailed weekly repeated assessments of emotional distress and pain over six months. Participants self-reported distress and pain via a mobile phone app (Upinion, Opinion Solutions (Pty) Ltd) using their personal or study-provided mobile phone (Mobicel FAME 16GB). The question battery was available in either English or isiXhosa (participant's choice). Current distress was assessed first, followed by questions on pain in the past week (reported here) and for the past three months (not reported here). Airtime compensation and a raffle system were used to incentivise participants to complete the weekly question battery. Upon weekly review of responses, non-responding participants were contacted telephonically to offer necessary technical support; participants reporting consistently high distress were offered information on local mental health services.

Approval for this study was obtained by the Human Research Ethics Committee of the University of Cape Town (approval number: 764/2019) and the City of Cape Town (ref: 24699). We followed the STROBE reporting guidelines [27] (Supplementary file). Details of the current study procedures are

listed in a protocol locked online [15]. Withdrawal from the study was permitted with no repercussions.

Procedure

Participants

The cohort for the current study was drawn from a primary study which included consenting adults with suppressed HIV who had consistently reported either persistent pain or no pain across the screening and baseline assessments for that study, and had no indication of psychiatric problems (see [15] for details). We invited all those people to opt into this cohort with no additional eligibility criteria, regardless of baseline pain status.

Outcomes

Pain

Pain-related questions were modified from the Brief Pain Inventory (BPI) [19] (Figure 1). Questions elicited information on pain presence/absence, anatomical site(s) of pain, anatomical site of the worst pain, and average and worst pain severity at the site of worst pain. Here, we use the questions asked about *pain in the past week*. Pain sites were reported on a body map divided into 18 regions, a similar approach to the Michigan body map [4]. Anatomical site name, colour, and number indicated the regions (Figure 2a). Pain severity (at the site of worst pain) was rated by selecting a number from 0 (no pain) to 10 (pain as bad as I can imagine) on a vertical visual & numerical scale (Figure 2b).

Emotional distress

Emotional distress was reported on a vertical visual & numerical scale in response to the question, "Throughout our lives, most of us feel distressed from time to time. Select the number between 0 and 10 that best describes how distressed you have felt, on average, over the past week." The scale ranged from 0-10, with 0 at the bottom of the scale indicating ‘not distressed at all’ and 10 at the

top, indicating 'as distressed as I could possibly be'. Participants could select any number from 0-10 (Figure 2c). The within-participant mean of distress scores (sum of distress scores divided by the count of distress scores) was taken forward to analysis.

[insert Figure 1 approximately here]

[insert Figure 2 approximately here]

Data analysis

This exploratory analysis visualised and statistically analysed distress and pain data reported over multiple weeks. The data collected on the mobile phone app were captured on Excel spreadsheets, weekly, with the date of assessment. The data were imported from the Excel spreadsheets and combined into a full dataset in R [25] (via RStudio [21]).

Data review and cleaning

The study ran for 49 weeks; each response was labelled with a number denoting the week in which that response was given. Week 1 began on the 16th of March 2021.

Data were excluded from seven participants due to data being inconsistent with eligibility criteria for the primary study (n = 6 screening and initial data collection questionnaires showed conflicting information on pain status, suggesting unreliable responding; and n = 1 participant was pregnant). We identified a further seven participants who had completed the survey more than once in one week. These responses were assessed for credibility. First, we compared the participant study identifier (PID) reported by the participant to the PID that had been assigned to the app-generated user number at study enrolment. Second, we assessed the consistency of responses across the weeks that preceded, included, and followed the week with multiple responses. Where there was clear consistency, the responses were flagged as duplicates, and the duplicate copy was removed (n = 4 responses). Inconsistent responses underwent logic checks, and subjective judgements were

used to establish whether distress or pain responses were realistic. Again, responses were removed in cases with reasonable doubt (n = 3 responses).

Descriptive statistics and plots

The median and interquartile range (IQR) were used to describe numerical data; frequency and proportion describe categorical variables. We descriptively and visually report the presence of pain, sites of pain and pain severity at the individual and group levels.

Statistical analysis

The goal of the current analysis was to develop a metric to capture variation in pain sites, after data inspection revealed the need for such a metric. The metric was intended to represent the total number of week-to-week changes in pain sites relative to the total number of week-to-week reports provided by the participant. Therefore, we included data from participants who had endorsed having pain at least once and, at a minimum, provided a response to the first question about pain in two consecutive weeks, during the study. We then proceeded using only those responses that were temporally consecutive to another response, within that participant (i.e. had a response in the immediately preceding week), and that therefore provided an opportunity to capture potential change in pain sites. In the pain sites variation metric, the numerator was the sum of all response-to-consecutive-response changes in all endorsed pain sites. The denominator was the count of opportunities to capture change, provided by the participant over the course of the study—which omitted the first response in each set of consecutive responses, since the first response alone does not provide an opportunity to capture change. For example, if a participant reported data in weeks 1, 2, and 5, site changes from weeks 1 to 2 contributed to the numerator, only week 2 contributed to the denominator count, and the data from week 5 did not contribute (see Table 1). If one response endorsed chest pain only, and the subsequent response endorsed head pain but not chest pain, that response-to-response change score was 2 and was summed with the other response-to-response

change scores for that participant to provide the numerator; that set of two consecutive responses contributed 1 to the denominator count (PID X1; Table 1).

[insert Table 1 approximately here]

First, we compared the metric with visualised individual endorsements of pain sites over time. Second, we assessed the range of the metric by plotting its distribution at the sample level, with four different cutoffs for participant inclusion. The purpose of this was to understand the metric's potential usefulness for studies with different numbers of repeated assessments. The cutoffs were informed by the data available; we used participants who had provided data with at least 1, 6, 11, or 21 opportunities to capture change. Third, we used Pearson's correlation test to assess whether the pain sites variation metric was associated with the mean of the count of painful sites (because more sites of pain should support more variability), the mean of worst pain severity, the standard deviation of worst pain severity (as a measure of variance in pain severity), or mean distress. We report the correlation coefficients (r) with 95% confidence intervals (CIs) and interpret p-values with an alpha of 0.05. We also performed a linear regression to assess whether associations shown to be significant with the tests of simple correlation remained so when adjusted for the mean of the count of painful sites. We report the estimates with 95% CI's and p-values at a threshold of 0.05. Fourth, to test whether these correlations differed systematically between people who contributed data with different numbers of opportunities to capture change, we conducted a weighted correlational analysis by assigning the data from each individual a weight according to the total number of opportunities to capture change in their data (e.g. the top contributor of 29 opportunities to capture change received a weight of 29/29 = 1; the lowest contributor of 1 opportunity to capture change received a weight of 1/29 = 0.034). We then compared the correlation coefficients between the weighted and unweighted analyses.

This analysis was conducted in R version 4.4.0 (R Foundation, Vienna, Austria) and RStudio (version 2024-04-24), using packages knitr [34], dplyr [31], tidyverse [30], gridExtra [1], magrittr [2], gtsummary [24], flextable [7], ggplot2 [32], patchwork [20], data.table [3], lubridate [8], forcats [29], fromatR [33], glue [11], sjPlot [13] and purr [9]. All participant data were de-identified for this analysis; the PIDs presented in the plots are different from the ones used during the data collection process.

Results

Description of all data

The study ran for 49 weeks and enrolled 72 adults. Most respondents were female (n = 51; 71%) and the median age (IQR) was 43 (37-51) years. In total, we received 1070 responses from these 72 participants. The number of responses provided by each participant ranged from 1-40. Only one participant provided 40 responses; the median (IQR) number of responses was 10 (5-17). Due to this variation in individuals' contributions to the overall dataset, we do not present participant-reported distress or pain variables at the level of the whole dataset because variable contributions per participant yield biased group-level data. Overall, 53 participants provided 2 or more consecutive responses including pain site data, across 49 weeks. That is, 53 participants provided 'opportunities to capture change' that were carried forward to the calculation of the pain sites variation metric.

Variation in the presence of pain

Figure 3 shows the opportunities to capture change provided by each participant over time (n=53). The median (IQR) number of opportunities to capture change provided by a participant over the course of the study was 10 (5-17). Over the course of the study, 5 participants reported the minimum of 1 opportunity to respond (PIDs 9, 20, 21, 43 & 47); 2 participants (PIDs 27 & 34) provided the highest number of 29 opportunities to capture change, both providing coverage of a continuous 30 week-period. Although all participants had been enrolled to the parent study after

reporting either no pain or persistent pain, in these weekly remote responses, endorsement of the presence of pain over opportunities to capture change was mostly inconsistent (note that data from a participant *never* endorsing pain would have been omitted for no opportunity to capture change). Only three participants (PIDs: 7, 34 & 41) reported pain in every consecutive week after their first response to the question. Nine participants (PIDs: 3, 18, 21, 22, 25, 29, 40, 47 & 53) were consistent in their endorsement of pain whenever they did respond but did not respond in every week after first responding. The remaining n = 42 had inconsistent pain status responses.

[insert figure 3 approximately here]

Pain sites

We saw marked intra-individual variations in pain sites over 49 weeks. From the 53 participants who provided data with opportunities to capture change, Figure 4a shows the count of endorsements of each possible number of unique pain sites (maximum 18) reported by each participant over the course of the study. It was most common for participants to endorse only two pain sites across the 49 weeks (n = 9), whereas five participants endorsed one pain site, and one participant endorsed every one of the possible 18 pain sites at some time during the study. Figure 4b shows endorsement rates for each of the 18 pain sites, at the group level - with endorsement of a site counted only once for each participant (n=53). The 10 most common pain sites endorsed at least once participants were head, upper back, lower back, upper arm, feet, pelvis and forearms (Figure 4b).

[insert Figure 4 approximately here]

Pain sites variation metric

The 53 participants who provided data with opportunities to capture change in the pain sites variation metric together provided 727 responses over the course of the study. Figures S2-S19 show the pain sites endorsed by each participant over time, along with their variability metric; Figure 5 shows three of these plots selected to represent participants with low, intermediate, and high

variability in pain sites. Of the 53 participants, 5 participants (e.g., PID 5; Figure 5a) reported a single site of pain; these participants and those who reported minimal week-to-week variability in pain sites had low variation metrics (e.g. Figure 5a). In contrast, 39 participants (e.g., PIDs: 14, 28) reported more than one site of pain at least once. Participants who frequently reported different sites, including over consecutive weeks, had higher variation metrics (e.g., Figure 5b & c). PID 28, who reported multiple, varying pain sites over time, had the highest variation metric in the sample (Figure 5c, variation metric = 5.11).

[insert Figure 5 approximately here]

Figure 6 shows the distributions of the pain sites variation metric based on the four different cutoffs for participant inclusion, which were greater than or equal to 1, 6, 11, or 21 opportunities to capture change. The range of the pain sites variation metric was consistent for cutoffs of 1, 6, and 11, at 0.18 to 5.11 (Figure 6a-d), but there was some difference in the distribution of the metric: the median (IQR) variation metric was higher for ≥21 week of responses (1.18 (0.42-1.92)) and lower for ≥11 weeks of responses (1.06 (0.45-1.92)). Few participants had a variation metric greater than 3 (n = 5 for ≥1 week; 4 for ≥6 weeks; n = 3 for ≥11 weeks and n = 1 for ≥21 weeks).

[insert Figure 6 approximately here]

Correlation analysis

Three participants had a mean distress rating of 10/10. The mean rating of worst pain was greater than 3/10 for most of the 53 participants; the most common mean rating of worst pain was 9/10 (n=9 of 53 participants) (Figure 7a). The most common within-participant mean distress rating across the number of opportunities to change pain sites was 6 or 8/10 (n = 7 each), followed by 4 (n = 6) (Figure 7b). Table 2 shows the Pearson's correlation test results from the unweighted and weighted analyses, at each subsample cutoff, for the relationships between the pain site variation metric and the within-participant mean of the count of painful sites, the within-participant mean of the worst

pain severity, the standard deviation of worst pain severity, or mean distress (also see Figures S19-S23). The pain sites variation metric was correlated with the mean of the count of painful sites at all cut-offs except at 21 opportunities for change. The metric was associated with the mean of ratings of worst pain, but only at the lower cutoffs (which retained more data) and with a small effect size, although the size of the correlation coefficient was reasonably stable (Table 2). This relationship was no longer significant when adjusted for the mean count of painful sites (Table 3). There was no evidence to support rejection of the null hypothesis that the pain sites variation metric is not associated with the standard deviation of ratings of worst pain.

The pain sites variation metric was positively and moderately associated with distress at all cutoffs except ≥21 weeks, where the correlation coefficient remained moderate, but the wide confidence interval suggested uncertainty. This association was also no longer significant once adjusted for the mean count of painful sites (Table 4). In general, the magnitudes of the correlations were similar in the unweighted and weighted analyses, suggesting that participants who provided more usable responses did not have an obviously different relationship of the number of pain sites to pain extent, worst pain, variance in worst pain, or distress.

[insert Figure 7 approximately here]

[insert Table 2 approximately here]

[insert Table 3 approximately here]

[insert Table 4 approximately here]

Discussion

This study aimed to develop a metric to describe and quantify intra-individual variation in pain sites for longitudinal pain studies. A secondary objective was to determine whether variation in pain sites, as captured by our pain site variability metric, was associated with pain extent, pain severity, variance in pain severity, or emotional distress. We drew on data from a cohort of 53 participants who, together, had provided 727 weekly reports of pain severity, pain site(s), and distress over 49 weeks. We found marked intra-individual changes in pain sites and pain severity between responses. The pain sites variation metric successfully captured the visualised intra-individual temporal variation in anatomical sites of pain by distinguishing participants with consistent pain sites from participants with high temporal variation in pain sites. The metric showed reasonable spread across the cohort. The pain sites variation metric was positively associated with the count of painful sites, suggesting, as expected, that people with more pain sites also had more variation in those sites. The metric was also associated with the mean of the worst pain severity in 2 of the 4 cutoffs and with emotional distress for 3 of the 4 inclusion cutoffs, but neither relationship remained when adjusted for the count of painful sites. The metric was not associated with variance in pain severity, and there was no obvious change in these relationships when they were weighted by the number of usable responses provided by each participant.

Variability in pain severity has recently received increased attention [5, 17], yet studies of variation in pain sites seem relatively uncommon. Besides the current study and the prior work that prompted it [28], we are aware of just one other dataset that has directly addressed intra-individual variation in pain sites [6]. That study collected pain site reports from people with chronic pelvic pain, 4 times a day for 14 days. A within-individual standard deviation in the count of pain sites over the study period represented intra-individual variability. However, this approach cannot capture both positive and negative changes in pain sites and may thus under-represent participants' lived experiences of change in pain sites. While we argue that a better metric is necessary for categorical data such as

pain sites, that study's finding of noteworthy intra-individual variation in pain sites supports our impression that there is a need to assess and understand variation in pain sites.

The significance of intra-individual variation in pain sites is not yet known. In our data, people with more sites of pain also had more variability in those pain sites. In line with the possibilities that apply to variation in pain severity and to the count of painful sites, variation in pain sites could be a meaningful clinical outcome or a predictor of other meaningful clinical outcomes. For example, is high variability in pain sites associated with greater impact of having pain, in people with chronic pain? Our analysis of suggests pain variability may not independently predict emotional distress; rather, our findings resemble other evidence that people with more sites of pain report more distress [12, 16, 26]. However, it remains possible that people living with pain do better when the bodily locations of their pain are more consistent; this is an outstanding question for direct engagement with people living with pain. Given the priority that many people with pain place on pain controllability and predictability, and the extra resources required to adjust to frequent changes in circumstances [18], reducing variation in pain sites may be important to people living with pain. However, we caution that most current work on pain controllability and predictability has implicitly focused on pain severity or interference, leaving a current shortage of previous research on pain *sites* to ground this idea.

Variation in pain sites seems particularly likely to influence other clinical outcomes, given that changes in pain sites are difficult to interpret and difficult to manage. We have observed that clinicians and patients have difficulty making sense of 'pain that moves', complicating diagnosis, treatment, and both psychological and functional coping. It would be worthwhile to directly investigate whether variation in pain sites predicts non-pain outcomes including psychological processes (e.g. pain-related worry or fear, hopelessness), mental wellbeing, functional goal attainment, and quality of life. The relationship of pain site variation to treatment responsiveness may also be worthy of attention. In clinical trials, high variability in pain severity at the baseline time

point has been associated with greater response to placebo interventions [23] and, conversely, smaller response to active pharmacological interventions [17], suggesting that high variability in pain severity could serve as a variable for enriching trial cohorts. Crucially, variation in pain sites has not received enough attention to clarify whether it, too, could predict responses to treatment. Alongside inquiry into prediction of non-pain variables, there is also a need to clarify how variation in pain sites relates to other pain variables such as severity of pain; although again, in our data, variation in pain sites was not independently associated with mean worst pain severity.

In the clinical context, variation in the sites of a person's pain often informs diagnostic and treatment decisions. Similarly, in the research context, pain site variation data has the potential to inform tentative deductions about putative causes of pain. For example, with reference to the current cohort of people with HIV, if a person reports bilateral foot pain but only feels it intermittently across consecutive weeks, we could reasonably rule out distal sensory neuropathy as a dominant cause. Similarly, if a person reports pain in one location and no pain in that location the following week, we would consider physical injury an unlikely cause of that pain. In this way, information on intra-individual variation in pain sites could support a degree of deductive reasoning that would be useful in interpreting data from large study cohorts where full diagnostic work-up is unavailable.

Limitations

The data from this cohort were reported remotely, which relies on participant responsiveness and offers limited opportunities for data validation. To support responses and identify misleading data, we engaged frequently with participants to provide training and ongoing support, called non-responders, checked on those reporting high distress or pain, and directed those in need to community services. To detect potential proxy reporting, we required respondents to enter their confidential study identification number and we cross-checked it against the number entered by the research team at app installation. Several participants commented on the intuitive nature of the

chat-like app interface. These strategies and feedback give us confidence that our data represent remote reporting on pain and distress by people with HIV from the real-life context of daily living. A second consideration pertains to the data on specific pain sites. The list of pain sites offered to participants began with the head, as indicated in Figure 2. It is possible that the high endorsement of the head as a pain site was biased by this presentation, if participants were unwilling to scroll down or simply gave the most convenient response. However, the reasonably high endorsement of the feet (response options 17 and 18) suggests that participants were generally willing to scroll down through the list of pain sites.

In this work, we have proposed that, alongside intra-individual variability in both pain severity and interference, intra-individual variation in pain sites may be an important measure of pain. We have provided a single metric to represent intra-individual variation in pain sites over time that captures both positive and negative changes at each bodily site and the frequency of those changes over time. An important limitation of the metric is its dependence on the number of anatomical sites into which the body is divided for the reporting task. In this study, participants could endorse up to 18 sites; a different number of possible sites would yield different numbers for the metric. This limits external comparison of the metric across studies with different methods. However, the metric seems well suited to within-study use to understand the relevance of variation in pain sites for wellbeing, given that our analysis was able to demonstrate that its relationship to emotional distress was removed by adjusting for the mean count of painful sites.

Future opportunities

The next challenges in understanding the importance of variation in pain sites are to investigate the extent to which this pain site variation matters to people living with pain, and to clarify whether it belongs in a causal chain modulating other outcomes or is a consequence of changes in other outcomes. Achieving this clarity will likely require intensive longitudinal study designs that provide high temporal resolution across multiple measures of pain and related factors such as psychological

wellbeing, social interactions, goal attainment, and healthcare experiences. Given the complex, interconnected nature of pain, it will be important to analyse real-time overlaps and intersections between factors using a biopsychosocial, whole-person perspective [10]. By capturing complex longitudinal information about intraindividual variation in pain sites in a single number, our metric of pain site variation is ideal to support such research questions.

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Table legends

Table 1. Examples responses from real and dummy participants (dummy PIDs indicated with X) to illustrate changes in pain sites from the preceding week and how the variation metric is calculated to reflect changes divided by opportunities to capture change.

Table 2: Correlations between the pain sites variation metric and the within-participant (a) mean of the count of painful sites, (b) mean of ratings of worst pain severity, (c) standard deviation of ratings of worst pain severity, or (d) distress ratings, using Pearson's correlation test and unweighted and weighted analyses, at each subsample cutoff. The asterisk (*) denotes a statistically significant correlation at alpha=0.05 (uncorrected).

Table 3: Linear regression of mean ratings of worst pain severity ("mean pain rating") predicting the pain sites variation metric, adjusted for the mean of the count of painful sites. Significant results at p <0.05 are shown in bold. CI = confidence interval.

Table 4: Linear regression of distress predicting the pain sites variation metric adjusted for the mean of the count of painful sites. Significant results at p <0.05 are shown in bold. CI = confidence interval.

Figure legends

Figure 1: Question flow. Exact phrasing is shown in Figure S1.

Figure 2: a) Body map, b) visual & numerical scale for pain severity and c) visual & numerical scale for distress.

Figure 3: Frequency of a) opportunities to capture change and b) presence of pain in the past week across 49 weeks. Orange colour: participant endorsed *pain* in the last week; green colour: participant endorsed *no pain* in the last week; white colour: weeks before a participant was enrolled into the study; grey colour: participant failed to respond *or* week without a response in the immediately preceding week). Study mobile phones were distributed to participants from 20 weeks into the study, to support participation. The number of opportunities to capture change for each participant is indicated on the far right with f (denoting frequency).

Figure 4: For all participants who provided data with opportunities to capture change, pain in the past week: a) count of endorsements of each possible number of pain sites b) the count of times each site was endorsed at least once by a participant. Numbers indicate endorsement counts.

Figure 5: Sites and severity of pain in the past week for 3 individuals (a-c). Each orange block shows an endorsed pain site, and the worst pain site is presented by a purple block; no pain site endorsed is indicated with a green block. Weeks with missing responses are shown in solid white.

Figure 6: Variation metrics for subsample defined by having provided data with opportunities to change (a) ≥1, (b) ≥6, (c) ≥11, or (d) ≥21 weeks.

Figure 7: a) Mean worst pain severity and b) mean distress scores, for each participant; usable responses only.

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Table 1. Examples responses from real and dummy participants (dummy PIDs indicated with X) to illustrate changes in pain sites from the preceding week and how the variation metric is calculated to reflect changes divided by opportunities to capture change.

		Head	Chest	Abdomen	Upper back	Left foot	Variation metric $\left(\frac{Number\ of\ changes}{Number\ of\ weeks}\right)$
PID 2	Week 42	✓	✗	✗	✓	✗	$\frac{5}{2+1} = 1.67$
	Week 43	✗	✗	✗	✗	✗	
	Week 44	✗	✗	✓	✗	✓	
	Week 46	✗	✗	✗	✗	✗	
	Week 47	✓	✗	✗	✗	✗	
PID X1	Week 42	✗	✓	✗	✗	✗	$\frac{2}{1} = 2.00$
	Week 43	✓	✗	✗	✗	✗	
PID X2	Week 32	✓	✗	✗	✗	✓	$\frac{6}{1+1} = 3$
	Week 33	✗	✓	✓	✗	✗	
	Week 35	✗	✗	✓	✓	✗	
	Week 36	✗	✓	✓	✓	✓	
PID X3	Week 34	✗	✗	✗	✗	✗	$\frac{2}{2} = 1$
	Week 35	✗	✗	✓	✗	✗	
	Week 36	✗	✗	✗	✗	✗	

Footnote: Ticks show endorsement of a site as painful; crosses show no endorsement. Green indicates a change in site within an opportunity to capture change, therefore contributing to the metric; orange shows a change in site within a response that is not an opportunity to capture change, i.e. a change in pain site that is not captured by the metric due to the absence of data from a week that temporally and immediately preceded that week.

Table 2: Correlations between the pain sites variation metric and the within-participant (a) mean of the count of painful sites, (b) mean of ratings of worst pain severity, (c) standard deviation of ratings of worst pain severity, or (d) distress ratings, using Pearson's correlation test and unweighted and weighted analyses, at each subsample cutoff. The asterisk (*) denotes a statistically significant correlation at alpha=0.05 (uncorrected).

	Pearson's r [95% CI]	
	unweighted analysis	weighted analysis
a) For mean of the count of painful sites		
≥1 opportunities to change (n=53)	0.84 [0.74 to 0.91]*	0.78 [0.64 to 0.93]*
≥6 opportunities to change (n=42)	0.79 [0.63 to 0.89]*	0.77 [0.55 to 0.98]*
≥11 opportunities to change (n=32)	0.80 [0.59 to 0.91]*	0.77 [0.51 to 1.02]*
≥21 opportunities to change (n=12)	0.67 [0.003 to 0.92]	0.063 [-0.14 to 1.39]
b) For mean of ratings of worst pain severity		
≥1 opportunities to change (n=53)	0.31 [0.04 to 0.54]*	0.29 [0.11 to 0.47]*
≥6 opportunities to change (n=42)	0.38 [-0.09 to 0.62]*	0.29 [0.08 to 0.50]*
≥11 opportunities to change (n=32)	0.29 [-0.07 to 0.58]	0.29 [0.02 to 0.56]*
≥21 opportunities to change (n=12)	0.26 [-0.37 to 0.72]	0.05 [-0.63 to 0.75]
c) For standard deviation of ratings of worst pain severity		
≥1 opportunities to change (n=53)	0.18 [-0.46 to 0.14]	-0.04 [-0.33 to 0.25]
≥6 opportunities to change (n=42)	-0.09 [-0.40 to 0.25]	-0.01 [-0.38 to 0.35]
≥11 opportunities to change (n=32)	-0.02 [-0.39 to 0.34]	-0.01 [-0.45 to 0.43]
≥21 opportunities to change (n=12)	0.21 [-0.70 to 0.41]	-0.10 [-0.74 to 0.94]
d) For mean of ratings of distress		
≥1 opportunities to change (n=53)	0.44 [0.19 to 0.63]*	0.46 [0.24 to 0.67]*
≥6 opportunities to change (n=42)	0.45 [0.17 to 0.66]*	0.51 [0.32 to 0.71]*
≥11 opportunities to change (n=32)	0.54 [0.23 to 0.75]*	0.50 [0.27 to 0.73]*
≥21 opportunities to change (n=12)	0.50 [-0.10 to 0.83]	0.36 [-0.18 to 0.91]

Table 3: Linear regression of mean ratings of worst pain severity ("mean pain rating") predicting the pain sites variation metric, adjusted for the mean of the count of painful sites. Significant results at p <0.05 are shown in bold. CI = confidence interval.

Model	Term	Estimate	95% CI	P-value
≥1 opportunity to change; n = 53	(Intercept)	0.79	[0.13 to 1.45]	**0.020**
	Mean pain rating	-0.01	[-0.11 to 0.09]	0.804
	Mean of the count of painful sites	0.57	[0.46 to 0.67]	**<0.001**
≥6 opportunity to change; n = 38	(Intercept)	0.61	[-0.22 to 1.43]	0.144
	Mean pain rating	0.01	[-0.12 to 0.13]	0.905
	Mean of the count of painful sites	0.55	[0.38 to 0.71]	**<0.001**
≥11 opportunity to change; n = 25	(Intercept)	0.78	[-0.71 to 2.26]	0.289
	Mean pain rating	-0.04	[-0.26 to 0.18]	0.733
	Mean of the count of painful sites	0.56	[0.36 to 0.77]	**<0.001**
≥21 opportunity to change; n = 9	(Intercept)	2.44	[-5.76 to 10.63]	0.494
	Mean pain rating	-0.26	[-1.24 to 0.73]	0.543
	Mean of the count of painful sites	0.78	[-0.03 to 1.60]	0.058

Table 4: Linear regression of distress predicting the pain sites variation metric adjusted for the mean of the count of painful sites. Significant results at p <0.05 are shown in bold. CI = confidence interval.

Model	Term	Estimate	95% CI	P-value
≥1 opportunity to change; n = 53	(Intercept)	0.52	[0.08 to 0.95]	**0.021**
	Mean distress rating	0.04	[-0.04 to 0.12]	0.269
	Mean of the count of painful sites	0.55	[0.44 to 0.66]	**<0.001**
≥6 opportunity to change; n = 38	(Intercept)	0.41	[-0.17 to 1.00]	0.161
	Mean distress rating	0.06	[-0.07 to 0.18]	0.345
	Mean of the count of painful sites	0.50	[0.31 to 0.69]	**<0.001**
≥11 opportunity to change; n = 25	(Intercept)	0.41	[-0.55 to 1.36]	0.385
	Mean distress rating	0.03	[-0.15 to 0.22]	0.709
	Mean of the count of painful sites	0.52	[0.28 to 0.75]	**<0.001**
≥21 opportunity to change; n = 9	(Intercept)	0.53	[-3.28 to 4.34]	0.745
	Mean distress rating	-0.04	[-0.65 to 0.57]	0.888
	Mean of the count of painful sites	0.75	[-0.28 to 1.78]	0.126

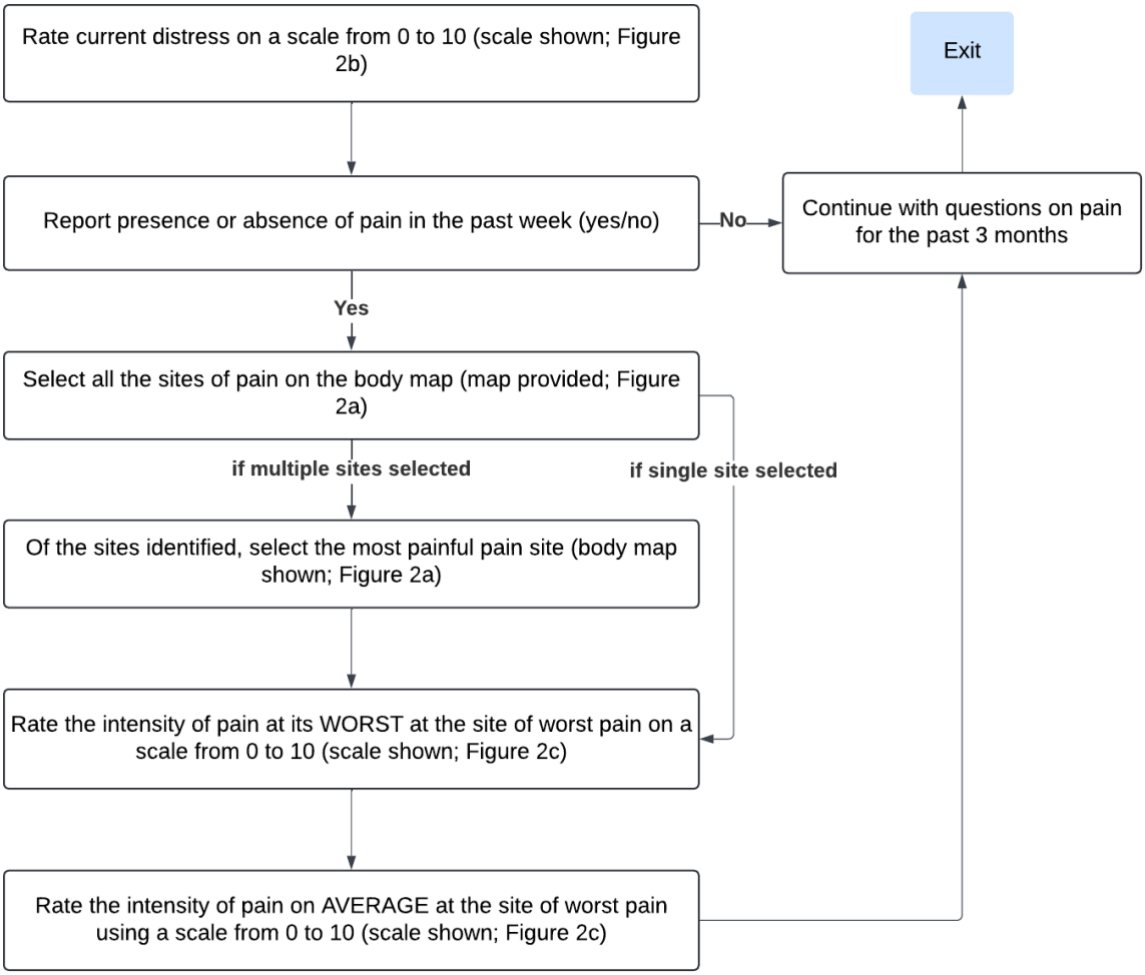

Figure 1: Question flow. Exact phrasing is shown in Figure S1.

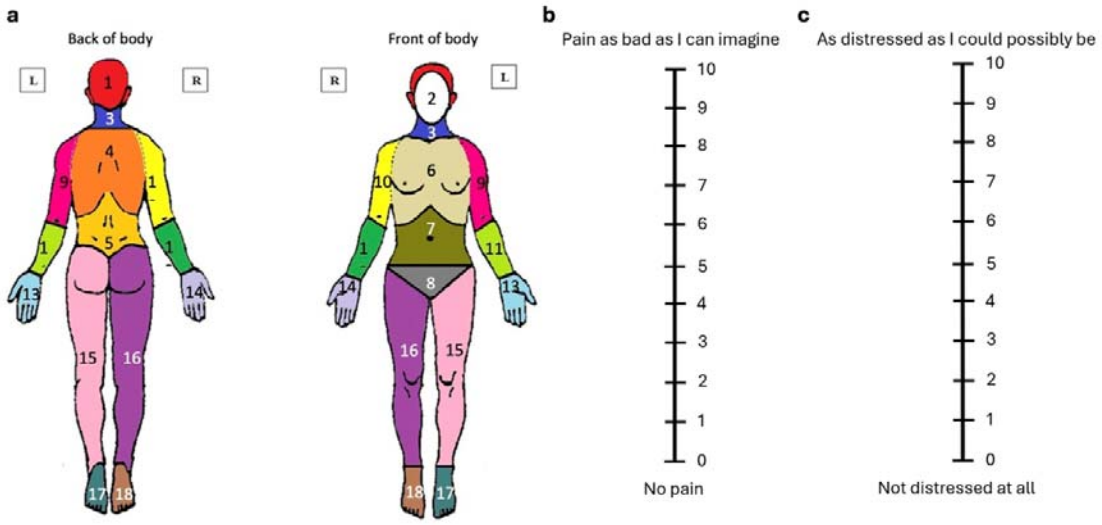

Figure 2: a) Body map, b) visual & numerical scale for pain severity and c) visual & numerical scale for distress.

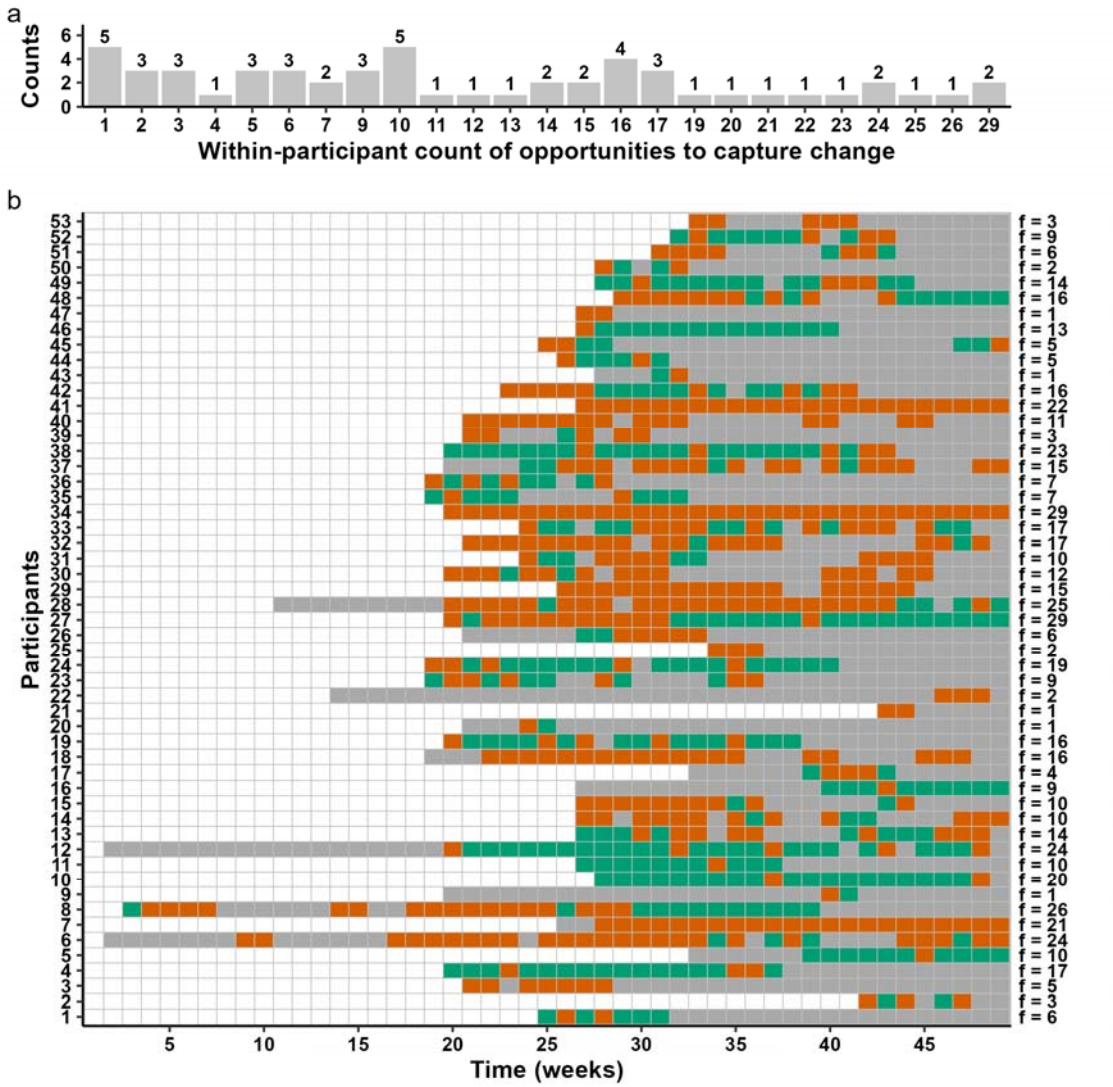

Figure 3: Frequency of a) opportunities to capture change and b) presence of pain in the past week across 49 weeks. Orange colour: participant endorsed pain in the last week; green colour: participant endorsed no pain in the last week; white colour: weeks before a participant was enrolled into the study; grey colour: participant failed to respond or week without a response in the immediately preceding week). Study mobile phones were distributed to participants from 20 weeks into the study, to support participation. The number of opportunities to capture change for each participant is indicated on the far right with f (denoting frequency).

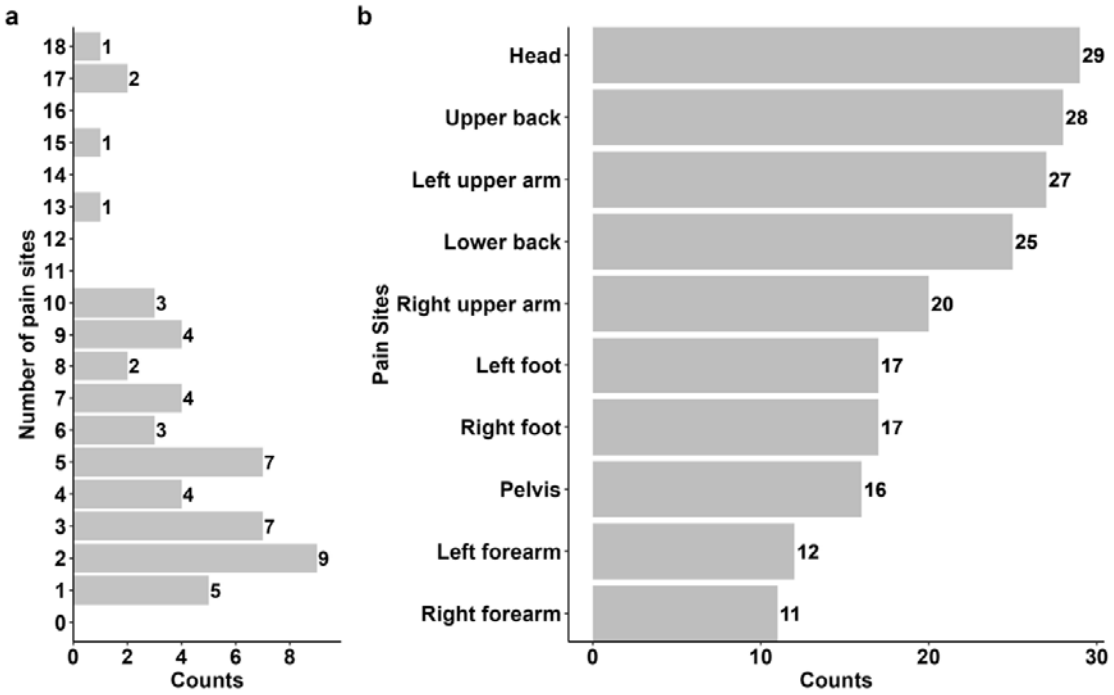

Figure 4: For all participants who provided data with opportunities to capture change, pain in the past week: a) count of endorsements of each possible number of pain sites b) the count of times each site was endorsed at least once by a participant. Numbers indicate endorsement counts.

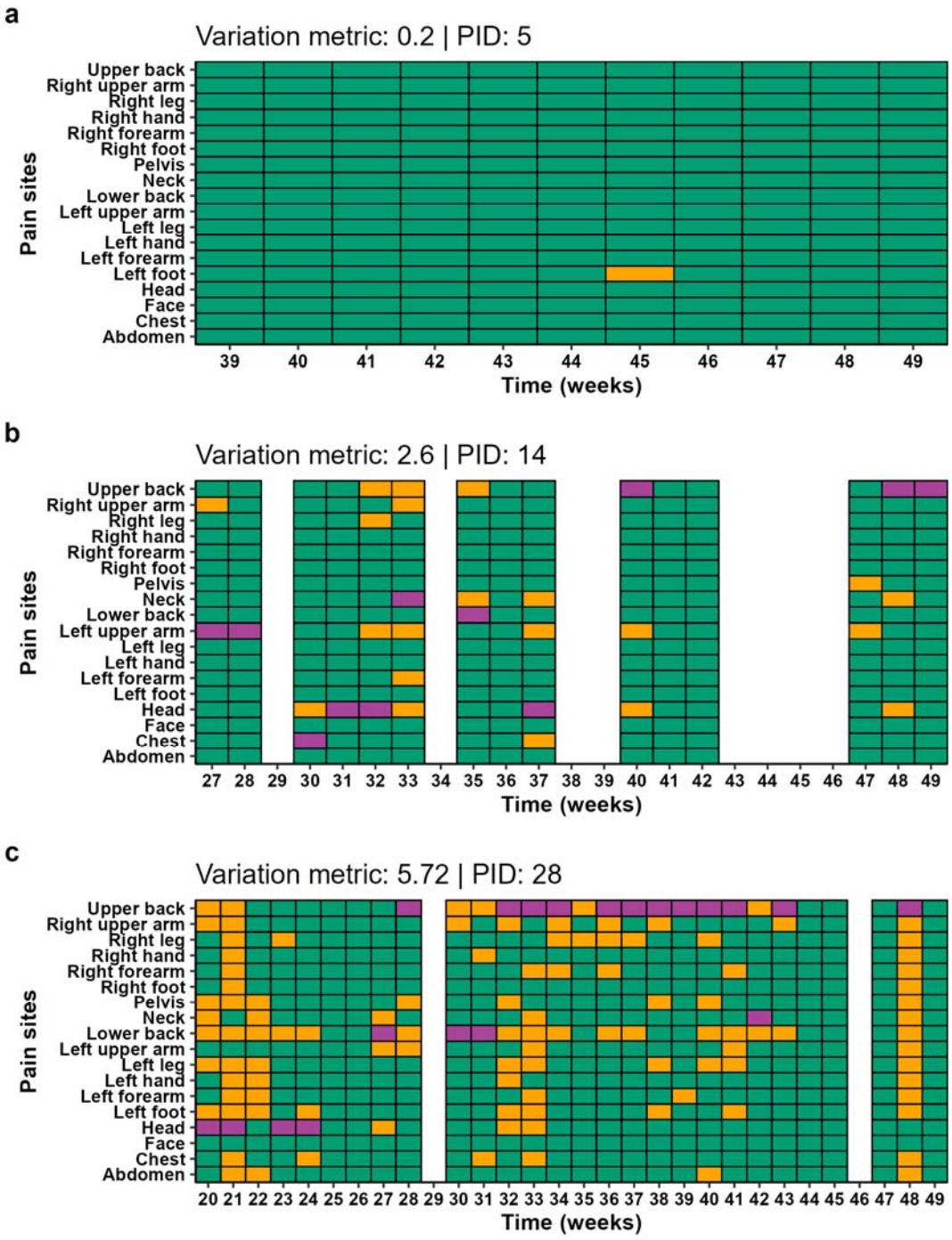

Figure 5: Sites and severity of pain in the past week for 3 individuals (a-c). Each orange block shows an endorsed pain site, and the worst pain site is presented by a purple block; no pain site endorsed is indicated with a green block. Weeks with missing responses are shown in solid white.

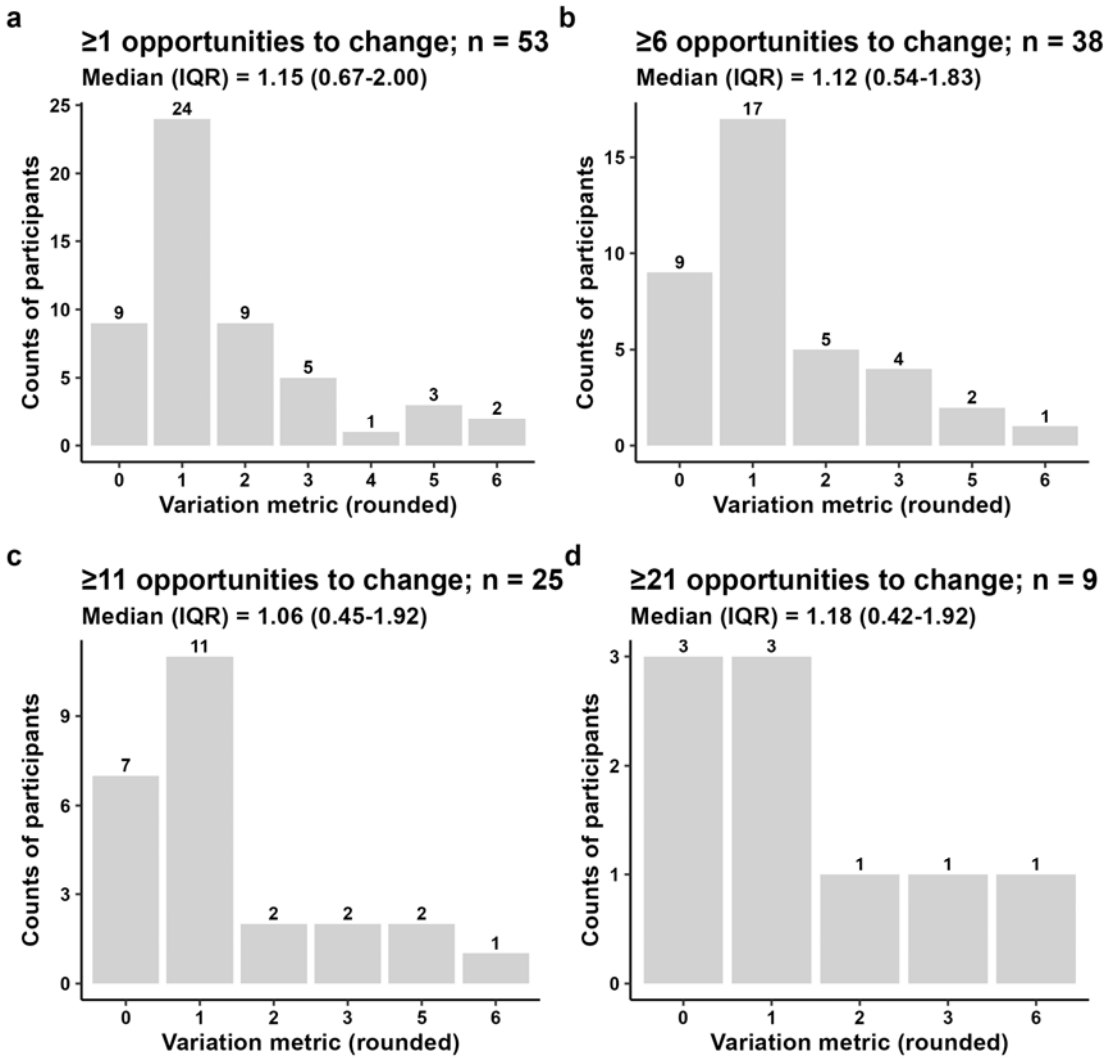

Figure 6: Variation metrics for subsample defined by having provided data with opportunities to change (a) ≥1, (b) ≥6, (c) ≥11, or (d) ≥21 weeks.

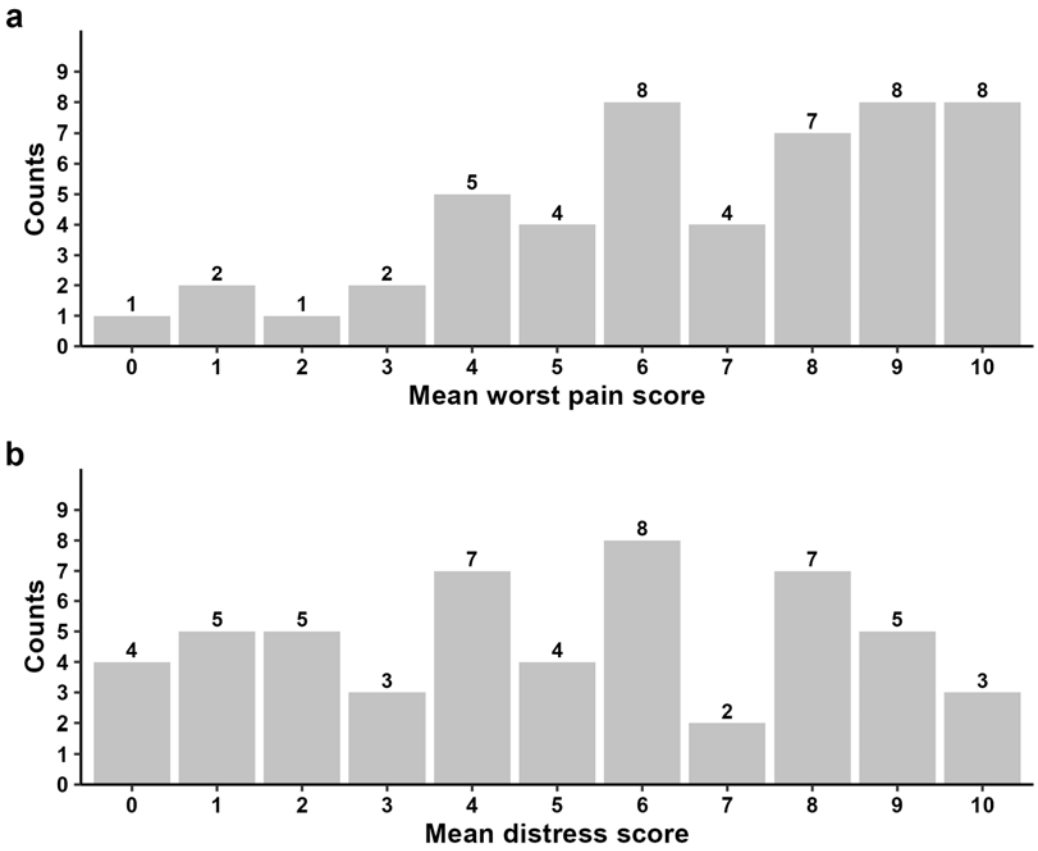

Figure 7: a) Mean worst pain severity and b) mean distress scores, for each participant; usable responses only.