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ORIGINAL REPORT

IMPACT OF EMOTIONAL DISTRESS AND PAIN-RELATED FEAR ON PATIENTS WITH CHRONIC PAIN: SUBGROUP ANALYSIS OF PATIENTS REFERRED TO MULTIMODAL REHABILITATION

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Objective: **Multimodal rehabilitation programmes (MMRP) for chronic pain could be improved by determining which patients do not benefit fully. General distress and pain-related fear may explain variations in the treatment effects of MMRP.**

Design: **Cohort study with a cross-sectional, prospective part.**

Patients: Chronic musculoskeletal pain patients referred to 2 hospital-based pain rehabilitation clinics.

Methods: **The cross-sectional part of this study cluster analyses patients (*n* = 1,218) with regard to distress and pain-related fear at first consultation in clinical pain rehabilitation and describes differences in external variables between clusters. The prospective part follows the subsample of patients (*n* = 260) participating in MMRP and describes outcome post-treatment.**

Results: **Four distinct subgroups were found: (*i*) those with low levels of distress and pain-related fear; (*ii*) those with high levels of pain-related fear; (*iii*) those with high levels of distress; and (*iv*) those with high levels of distress and pain-related fear. These subgroups showed differences in demographics, pain characteristics, quality of life, and acceptance, as well as the degree of MMRP participation and MMRP outcome.**

Conclusion: **Among patients with chronic pain referred to MMRP there are subgroups with different profiles of distress and pain-related fear, which are relevant to understanding the adaptation to pain and MMRP outcome. This knowledge may help us to select patients and tailor treatment for better results.**

Key words: chronic pain; rehabilitation; multidisciplinary pain clinic; fear avoidance beliefs; distress; profiles; Swedish Quality Registry for Pain Rehabilitation.

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The bio-psycho-social (BPS) model has been adopted for the management of patients with chronic pain because there is good evidence that medical, psychological and social factors affect the development and maintenance of chronic pain (1). Multimodal rehabilitation programmes (MMRP) are the clinical application of the BPS paradigm and show significant results on a group level (2–5). However, while MMRP are generally effective, there is large variation in effect, and the effect sizes are at best moderate (2, 5). This raises the question as to what characterizes patients who do not benefit fully from MMRP.

There are a number of psychological factors that contribute to the development and maintenance of pain (6–8), e.g. general emotional distress and pain-related fear. Psychological theories suggest how these risk factors interrelate and relate to poor outcome. The fear avoidance theory, the theory of misdirected problem-solving and the shared vulnerability model are examples of theories that have somewhat different emphases, but link together with emotion regulation as a unifying factor (9–11). These theories focus on how cognitive, emotional and behavioural responses to the perception of threat (e.g. worry, fear, avoidance), as well as vulnerabilities for these responses, may help to explain variations in adaptation to pain.

Based on these theories, the emotional profiles of patients with pain may influence outcome. In a study investigating outcome in cognitive behaviour therapy informed pain management, 56% of patients with pre-treatment anxiety problems did not improve (12). Moreover, studies suggest the importance of investigating subgroups with different combinations of psychological risk factors (13, 14). Some studies indicate that patients with a combination of risk factors, such as high levels of emotional distress and poor pain coping, may have an elevated risk of poor outcome (8, 15, 16). This implies that different emotional profiles could explain variations in outcome of MMRP. However, previous studies have used small samples and have not specifically studied patients with chronic pain referred to rehabilitation specialist care. There is a need to replicate these studies in a larger sample with a clinically relevant group of patients with chronic pain seeking rehabilitation care.

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Patients registered in the Swedish Quality Registry for Pain Rehabilitation (SQRP) (17) represent a large and clinically relevant patient group. By using SQRP data from 2 large pain rehabilitation centres and profiles of patients based on their level of general emotional distress and pain-related fear at first consultation, this study aims to investigate whether and how hypothesized subgroups of a representative chronic pain sample differ in terms of participation in, and outcome of, an MMRP. Specifically, the aim was to investigate whether different profiles for pain-related fear and distress were related to demographics, pain characteristics, quality of life and acceptance, the likelihood of entering a MMRP, and MMRP outcome.

METHODS

Design

This is a cohort study with a cross-sectional and prospective part (Fig. 1). The cross-sectional part describes patients at first consultation to the pain rehabilitation centre, and the prospective part follows those patients who continue on to participate in MMRP and describes results at post-treatment.

Before the first consultation, patients received written information about the study, and signed a consent form in accordance with the principles of the Declaration of Helsinki. This study was granted ethical clearance by the Umeå University Ethics Committee (Dnr: 2013/192-31).

Subjects and setting

Subjects are 1,218 (70%) out of 1,735 consecutive patients with chronic musculoskeletal pain conditions, age range 18–65 years, who during 2008–2012 were referred to the 2 clinical departments at the University Hospitals of Linköping (i.e. the Pain and Rehabilitation Centre) and Umeå (i.e. the Pain Rehabilitation Clinic) and who reported data to the SQRP. Patients report data by completing a paper and pencil questionnaire that is thereafter transferred to the SQRP electronic database. Approximately 98% of all referred patients deliver data. The SQRP is a Swedish national registry mainly based on questionnaires completed by the patients before and after MMRP.

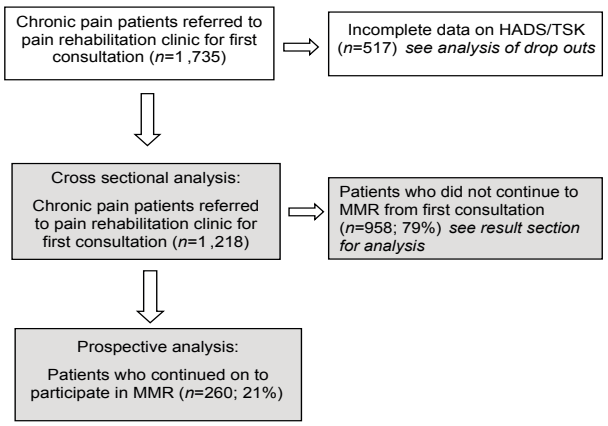

Fig. 1. Flow chart of patients in the study. HADS: Hospital Anxiety and Depression Scale; TSK: Tampa Scale for Kinesiophobia; MMR: Multimodal rehabilitation.

Multimodal rehabilitation

All referred patients received multimodal assessment by a physician alone or together with a psychologist, an occupational therapist or a physiotherapist. The MMRP was conducted in groups of 6–9 participants and included physiotherapy, ergonomics, training in coping strategies as well as education in pain management. The MMRP at both sites lasted for 6–8 weeks. Waiting time after first referral was approximately 4–8 weeks; the period between first assessment and post-treatment assessment was therefore in the range 10–16 weeks. Inclusion criteria and MMRP content have been described in detail elsewhere (18).

Analysis of drop-outs

A total of 1,218 out of 1,735 (70%) patients had complete data on the SQRP variables used for subgrouping, Hospital Anxiety and Depression Scale (HADS) (19) and the Tampa Scale for Kinesiophobia (TSK) (20), and were included in the analyses. The patients ($n=517$) who were excluded due to missing data on these variables did not differ in terms of age, sex and pain duration, but had small, but significantly, lower levels of pain intensity (mean 4.4, SD 0.9) and pain interference (mean 4.4, SD 1.1) compared with the included patients (pain intensity; mean 4.6 (SD 0.9); $t(1,642)=3.9$, $p<0.001$); pain interference; mean 4.6 (SD 1.0); $t(1,629)=2.9$, $p<0.001$).

Measures (all measures are included in the SQRP)

Demographic variables. Assessed demographics included: age; sex; country of birth (% born in Sweden); education (% post-upper secondary education).

Pain characteristics. Assessed pain characteristics included: Healthcare visits (% >4 visits a year); Pain duration (years); Pain location (presence of pain in 36 predefined anatomical areas. The number was calculated and labelled the Pain Region Index (PRI, range 0–36)).

West Haven-Yale Multidimensional Pain Inventory ((WHY) MPI). The (WHY) MPI is a psychometrically sound, 61-item self-report questionnaire measuring psychosocial, cognitive, and behavioural effects of chronic pain (21, 22). It is divided into 3 sections whereof parts of sections 1 and 3 where used as descriptive and outcome variables in this study. Specifically, we used the Pain severity (MPI-Pain-severity) and Interference – pain-related interference in everyday life (MPI-Pain-interference) subscales of section 1 and the General Activity Index (MPI-GAI) of section 3. We only used the General Activity Index of the items of section 3 due to lack of validity of the single items of this part in the Swedish context (23).

Furthermore, to validate our subgroups, we used the 3 subgroups that can be extracted from the MPI. In short, MPI identifies adaptive copers (AC), dysfunctional (DYS) and interpersonally distressed (ID). AC patients are characterized by low pain severity, pain interference and affective distress, high perception of life control and activity level. The DYS patients have high pain severity, interference and affective distress, low life control and activity level. ID patients are characterized by lower levels of social support, solicitous and distracting responses from significant others and higher levels of punishing responses compared with AC and DYS patients (24).

Tampa Scale for Kinesiophobia (TSK). Pain-related fear was assessed with the TSK (20). The 17 items are rated on a 4-point numerical scale, ranging from 1 (strongly disagree) to 4 (strongly agree) (range 17–68). Scores over 35 can be seen to indicate problematic pain-related fear (25). The TSK has shown to be a reliable assessment tool in chronic pain populations with a stable factor structure across pain diagnoses and nationalities (26, 27).

Hospital Anxiety and Depression Scale (HADS). Emotional distress was assessed with the HADS (19). The 14 items are rated on 4-point numerical scale (end-points varying with the statement) and summed into a 7-item depression and anxiety subscale (HAD-D and HAD-A; range 0–21): However, the 14 items can also be added to form a composite score measuring general emotional distress (range 0–42). HADS-A and HADS-D scores > 10 have shown to indicate problems on a clinical level (19). The HADS subscales and the total scale have been found to have good psychometric characteristics (28, 29).

Chronic Pain Acceptance Questionnaire (CPAQ). Acceptance behaviours and attitudes towards pain were assessed with the CPAQ (30). The 20 items are rated on a numerical scale from 0 (never true) to 6 (always true) and summed into 2 subscales: activity engagement (CPAQ-engagement; range 0–66) and pain willingness (CPAQ-willingness; range 0–54) The CPAQ has shown to be reliable and valid both in the English and Swedish versions (30, 31).

European Quality of Life instrument (EQ-5D). Perceived health was assessed with the EQ-5D (32). EQ-5D encompasses an index as well as a global self-estimate of health on a 100-point, thermometer-like scale (EQ-5D VAS; high values indicate good health and low values indicate poor health). Only the EQ-5D VAS scale was used for this study. The EQ-5D has shown adequate validity and responsiveness for patients with chronic pain (33).

Statistical analysis

All statistical analyses were performed using IBM SPSS Statistics (version 22.0). Up to 20% missingness (2 items) was accepted within each measure. Missing items were replaced with mean values. Cases with missing values on a measure were excluded from the analysis concerning that particular measure.

Cluster analysis was used to extract subgroups of patients with similar scoring patterns on pain-related fear (TSK), and emotional distress (total HADS score). As traditional statistical analyses may hide the existence of subgroups with different patterns of distress and pain-related fear, a cluster analytical approach was used as a methodological tool. An advantage of this approach is that it allows for a mapping of the co-occurrence of distress and pain-related fear on an individual level. It also provides the opportunity to study the comorbidity of symptoms that some individuals may experience in relation to the characteristics of hypothetical subgroups of individuals that have singular or no symptoms. Squared Euclidean distance was used as the similarity measure and Ward's method to minimize within-cluster differences. A cluster solution that explained at least 67% of the total error sum of squares was selected for additional k-means cluster analysis using hierarchical analysis centre points as point of departure. This additional analysis maximizes the homogeneity of the clusters by allowing cases to move to a better fitting cluster. Analysis of variance (ANOVA) (Tukey's b as *post-hoc* test) and χ^2 tests (z-tests to compare proportions) were used to compare the clusters on demographics, pain intensity, pain interference, perceived health and pain acceptance. For the cross-sectional sample, the clusters were also compared on MPI dysfunctional, interpersonal and adaptive coping scale scores. For the subsample continuing for rehabilitation treatment, repeated measures ANOVA (Games-Howell as post-hoc test, including 95% CI and effect size (η^2)) were used to analyse changes from assessment to post-treatment. One-way ANOVAs were used to test subgroup differences at post-treatment.

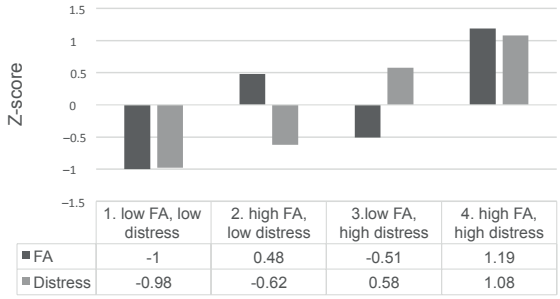

Fig. 2. Subgroup levels of pain-related fear and distress relative to one another. Y-axis represents Z-scores. FA: pain-related fear as measured with the Tampa Scale for Kinesiophobia; Distress: as measured with the Hospital Anxiety and Depression Scale total scale.

RESULTS

Subgroups of distress and pain-related fear: description and validation.

Cluster analysis of scores on the TSK and HADS total scale gave 4 distinct subgroups. Fig. 2 gives a visual display of the subgroups relative to one another and Table I describes the subgroups on the TSK, HADS scales, and the MPI adaptive coping, interpersonal and dysfunctional scales for validation purposes.

Table I. Validation of subgroups

	1. Low FA, low distress	2. High FA, low distress	3. Low FA, high distress	4. High FA, high distress	F
Number (% of total 1,218)	322 (26.4%)	317 (26.0%)	319 (26.2%)	260 (21.3%)	
Anxiety (HADS)	4.0 (2.6)[a]	5.7 (2.9)[b]	10.8 (3.2)[c]	13.4 (3.3)[d]	625.85 (3, 1,214)*
Depression (HADS)	4.4 (2.8)[a]	5.7 (2.7)[b]	10.7 (3.2)[c]	12.2 (3.5)[d]	461.17 (3, 1,214)*
Pain-related fear (TSK)	30.1 (4.7)[a]	43.5 (4.9)[b]	34.4 (4.6)[c]	49.7 (5.5)[d]	951.92 (3, 1,214)*
Adaptive coping (MPI)	61.2 (39.7)[a]	39.7 (37.7)[b]	15.4 (26.6)[c]	6.3 (15.5)[d]	161.56 (3, 1,088)*
Interpersonal coping (MPI)	17.1 (30.5)[a]	20.1 (32.8)[a]	41.0 (43.0)[b]	28.1 (38.6)[c]	24.52 (3, 1,088)*
Dysfunctional coping (MPI)	21.6 (33.0)[a]	40.0 (40.2)[b]	43.6 (42.4)[b]	65.6 (40.6)[c]	54.98 (3, 1,088)*

*$p < 0.001$. Different superscript letters noted after mean (and standard deviation; SD) indicate significant *post-hoc* test differences between subgroups. Where superscripts are the same the *post-hoc* tests did not indicate any significant differences between the respective subgroups. HADS: Hospital Anxiety and Depression Scale; TSK: Tampa scale for Kinesiophobia; MPI: Multidimensional Pain Inventory; FA: pain-related fear as measured with the Tampa Scale for Kinesiophobia.

First, there is a subgroup with relatively low scores on both measures. In comparison with benchmarks for clinical significance (see Methods), this subgroup has low levels of pain-related fear, anxiety and depression. This subgroup scores significantly higher than the other groups on the adaptive coper subscale of the MPI.

Secondly, there is a subgroup with relatively high scores on the TSK, but low scores on the HADS. This subgroup scores above the benchmark for high levels of pain-related fear, but not for anxiety and depression. This subgroup also scores relatively high on the adaptive coper subscale of the MPI, compared with the third and fourth subgroup.

Thirdly, there is a subgroup with relatively low scores on the TSK, but high on the HADS. This subgroup scores above the benchmark for anxiety and depression, indicating clinically significant emotional problems, but below the benchmark for problematic pain-related fear. This subgroup scores significantly higher on the interpersonal subscale of the MPI, compared with the other subgroups.

Fourthly, there is a subgroup with relatively high scores on the TSK as well as on the HADS. This subgroup scores above the benchmark for anxiety and depression as well as for pain-related fear, indicating clinically significant problems in both areas. This subgroup scores significantly higher on the dysfunctional coping subscale of the MPI, compared with the other groups.

Are there differences between subgroups on external variables?

Table II gives the characteristics of the subgroups on demographics and other relevant measures. The subgroups differ significantly on all variables but age. Compared with the other groups, the subgroup with a combination of high distress and high pain-related fear includes a relatively lower proportion of women and individuals born in Sweden. In addition, this subgroup (as well as the subgroup with only high pain-related fear) has a lower proportion of individuals with a higher education. This subgroup also reports significantly more use of healthcare, and shows the lowest levels of perceived health, willingness to experience pain and engagement in activity.

Are there differences between patients continuing and not continuing to MMRP?

Of the 1,218 patients, 260 patients (21%) went on to MMRP. A higher proportion of females continued on to participate in MMRP (24% of females vs 14% of males; χ^2 (1) = 15.5, $p < 0.001$). Moreover, those who continued to participate in MMRP were significantly younger (mean 39.4, SD 10.2 vs mean 41.6, SD 11.9; t(471.4) = 3.0, $p = 0.003$) and had slightly, but significantly, lower pain intensity (mean 4.3, SD 0.9 vs mean 4.5, SD 0.9; t(1,211) = 2.8, $p = 0.006$). There were no significant differences in pain interference or pain duration. Lastly, there were significant differences in level of pain-related fear, but not anxiety and depression, between those who did or did not participate in MMRP. Those who did not participate had a significantly higher level of pain-related fear (mean 39.3, SD 9.2) compared with those who did (mean 37.6, SD 8.0; t(459.9) = 2.9, $p = 0.004$). However, a closer look on a subgroup level shows that there were differences between the subgroups in the proportion of patients who continue on to MMRP. Specifically, from the subgroup with high scores on pain-related fear and distress fewer patients (15%) continued on to MMRP compared with the subgroup with high pain-related fear, but low distress (27%; χ^2 (3) = 13.09, $p < 0.01$).

Table II. Cross-sectional analysis of differences between subgroups

	Total sample	1. Low FA, low distress	2. High FA, low distress	3. Low FA, high distress	4. High FA, high distress	F/χ^2
Sex (% women)	73	79[a]	72[a]	79[a]	59[b]	37.25 (3)*
Born in Sweden (% yes)	89	98[a]	91b	93[b]	72[c]	108.54 (3)*
Age, years, mean (SD)	42.2 (11.6)	40.8 (10.9)	41.7 (12.1)	40.1 (11.8)	42.2 (11.5)	NS
Education (% post-gymnasium education)	25	31[a]	24[a,b]	33[a]	15[b]	27.80 (3)*
Healthcare usage (% ≥4 visits past year)	62	53[a]	64[a]	57[a]	74[b]	29.28 (3)*
Continue MMRP (% yes)	21	20[a,b]	27[b]	23[a,b]	15[a]	13.09 (3)*
Pain intensity (MPI; 0–6; $n = 1,213$)	4.4 (0.9)	4.0 (0.9)[a]	4.4 (0.9)[b]	4.4 (0.8)[b]	5.0 (0.7)[c]	63.09 (3, 1,209)*
Pain localization (PRI; 0–36; $n = 1,218$)	13.8 (8.2)	12.2 (7.8)[a]	13.2 (8.1)[a]	15.0 (8.3)[b]	15.1 (8.3)[b]	9.22 (3, 1,214)*
Interference (MPI; 0–6; $n = 1,211$)	4.4 (1.1)	3.7 (1.1)[a]	4.3 (0.9)[b]	4.7 (0.9)[c]	5.1 (0.7)[d]	106.03 (3, 1,207)*
Engagement (CPAQ; 0–66; $n = 1,064$)	26.7 (12.3)	34.1 (10.4)[a]	27.2 (11.8)[b]	25.7 (10.5)[b]	18.8 (12.0)[c]	79.88 (3, 1,060)*
Willingness (CPAQ; 0–54; $n = 1,088$)	23.0 (8.7)	29.1 (7.7)[a]	22.1 (7.8)[b]	23.0 (7.7)[b]	17.3 (7.9)[c]	102.64 (3, 1,084)*
Perceived health status (EQ-5D VAS; 0–100; $n = 1,166$)	41.8 (19.8)	51.5 (20.0)[a]	43.2 (18.1)[b]	39.2 (17.6)[c]	31.4 (18.3)[d]	56.89 (3, 1,162)*

*$p < 0.001$. Different superscript letters after mean (and standard deviation; SD) or % indicate significant *post-hoc* test differences between subgroups. Where superscripts are the same the *post-hoc* tests did not indicate any significant differences between the respective subgroups.
MMRP: Multimodal rehabilitation programmes; MPI: Multidimensional Pain Inventory; PRI: Pain Region Index; CPAQ: Chronic Pain Acceptance Questionnaire; EQ-5D: European Quality of Life instrument; VAS: Visual analogue scale FA: pain-related fear as measured with the Tampa Scale for Kinesiophobia.

Differences in treatment outcome

On the overall group level, patients significantly improved on pain intensity (Mdiff (95% CI)=–0.36 (–0.48; –0.24); F(1, 254)=34.1, $p<0.001$; $\eta^2=0.12$), pain interference (Mdiff (95% CI)=–0.38 (–0.48; –0.28); (F(1, 254)=58.6, $p<0.001$; $\eta^2=0.18$), perceived health status (Mdiff (95% CI)=9.16 (6.44; 11.89); F(1, 238)=43.9, $p<0.001$; $\eta^2=0.16$), willingness to experience pain (Mdiff (95% CI)=2.88 (1.86; 3.91); F(1, 223)=30.7, $p<0.001$; $\eta^2=0.12$) and activity engagement (Mdiff (95% CI)=5.52 (4.32; 6.73); F(1, 208)=81.7, $p<0.001$; $\eta^2=0.28$). These changes were independent of subgroup.

Changes in anxiety (F(3, 256)=22.2; $p<0.001$; $\eta^2=0.21$), depression (F(3, 256)=10.0; $p<0.001$; $\eta^2=0.11$), and pain-related fear (F(3, 238)=25.9; $p<0.001$; $\eta^2=0.25$), were dependent on subgroup. Specifically, magnitude of change in anxiety and pain-related fear was significantly different between all subgroups, while magnitude of change in depression was significantly different in subgroups 3 and 4 compared with subgroups 1 and 2. In general, the subgroups with high levels of distress and/or pain-related fear improved most on these variables, while the subgroups that were low on these factors did not improve.

Table III displays descriptives and analyses of subgroup differences on post-treatment outcome variables for those patients who continued on to MMRP. Differences remain between the subgroups on all but perceived health status ($p=0.07$). Post-treatment levels of distress for the subgroups with distress only (subgroup 3), and the subgroup with distress and pain-related fear (subgroup 4) are in the zone of a "possible case" according to criteria, indicating residual problems with distress. Post-treatment mean levels of pain-related fear for the subgroups with pain-related fear and avoidance only (subgroup 2), and the subgroup with distress and pain-related fear (subgroup 4) are around the benchmark for problematic levels of pain-related fear, indicating residual problems with pain-related fear.

DISCUSSION

The results of this study show that patients with chronic pain referred to MMRP in specialist care have different profiles of emotional distress and pain-related fear that could be of relevance for understanding their adaptation to pain and MMRP outcome. The 4 emotional subgroups showed marked differences in function, perceived health and healthcare usage, as well as MMRP outcome and proportion who went on to MMRP. The results replicate and extend findings from earlier studies using similar profiling variables, but different pain populations (14, 15).

There were also differences in demographic characteristics between the subgroups. The subgroups with high levels of pain-related fear had relatively lower education level. This is in line with the literature showing that fear and avoidance beliefs are related to lower educational level (34). Furthermore, the subgroup with high distress and pain-related fear included a higher proportion of men and patients born outside of Sweden. This highlights the importance of socio-demographic factors that may correlate with the outcome of MMRP and adds recent findings showing that socio-demographic factors may predict outcome of MMRP (35).

These results converge on other models classifying patients' coping with pain, e.g. on classic MPI profiles that divide patients in 3 subgroups: dysfunctional, interpersonally distressed or adaptive copers (24). Patients with high levels of pain-related fear in combination with emotional distress (group 4) converge most clearly on the MPI profile of dysfunctional coping, while patients with similar levels of emotional distress, but low pain-related fear (group 3), score highest on

Table III. Descriptives of treatment outcome for patients in the different subgroups who continued on to MMRP

	1. Low FA, low distress	2. High FA, low distress	3. Low FA, high distress	4. High FA, high distress	F
Number (% of total 260)	64 (24.6)	84 (32.3)	74 (28.5)	38 (14.6)	
Anxiety (HADS)	5.0 (2.8)[a]	6.5 (3.3)[b]	8.1 (4.1)[c]	9.1 (3.8)[c]	13.32 (3, 256)*
Depression (HADS)	4.8 (3.2)[a]	5.7 (3.0)[a]	7.8 (4.7)[b]	8.7 (3.8)[b]	12.95 (3, 256)*
Fear avoidance beliefs (TSK)	29.9 (5.4)[a]	37.3 (5.7)[b]	31.9 (5.8)[a]	39.1 (6.9)[b]	29.36 (3, 238)*
Pain intensity (MPI)	3.6 (1.0)[a]	4.0 (1.1)[a,b]	4.0 (1.0)[a,b]	4.4 (1.1)[b]	3.91 (3, 256)*
Interference (MPI)	3.7 (1.0)[a]	4.1 (.9)[b]	4.1 (1.0)[b]	4.6 (.9)[c]	8.08 (3, 256)*
Engagement (CPAQ)	37.5 (9.3)[a]	31.1 (10.1)[b]	32.9 (10.7)[b]	24.4 (10.2)[c]	12.63 (3, 232)*
Willingness (CPAQ)	30.0 (7.4)[a]	25.0 (7.0)[b]	26.2 (7.6)[b]	20.9 (7.1)[c]	12.12 (3, 238)*
Perceived health status (EQ-5D VAS)	54.9 (17.5)[a]	49.0 (20.2)[a,b]	48.0 (19.6)[a,b]	44.4 (23.8)[b]	2.39 (3, 247) ns (0.07)

*$p<0.001$. Different superscript letters after mean (standard deviation; SD) indicate significant *post-hoc* test differences between subgroups. Where superscripts are the same, the *post-hoc* tests did not indicate any significant differences between the respective subgroups.
HADS: Hospital Anxiety and Depression Scale;MMRP: Multimodal rehabilitation programmes; MPI: Multidimensional Pain Inventory; CPAQ: Chronic Pain Acceptance Questionnaire; EQ-5D: European Quality of Life instrument; VAS: Visual analogue scale FA: pain-related fear as measured with the Tampa Scale for Kinesiophobia.

the MPI profile of interpersonal distress. As expected, the subgroup with relatively low levels of distress and pain-related fear converges most on a profile of adaptive coping. This validates the subgroups found in this study using the established descriptive framework of the MPI, but also extends the understanding of the MPI subgroups by giving them a theoretical context.

The results also converge on the more recent acceptance-oriented models of adaptation to pain (36). More specifically it is the subgroup with the highest levels of emotional distress and pain-related fear that displays the lowest levels of pain acceptance. Indeed, studies have shown that acceptance of pain and fear of pain are inversely related to one another (37). Thus, the results of this study may bridge and integrate some of the parallel literature on pain acceptance and pain-related fear by showing that these descriptions of patients may be seen as 2 sides of the same coin.

The differences between the subgroups on distress, on the one hand, and pain-related fear, on the other hand, highlight the possible interaction between general emotional reactivity and pain-related fear in the development and maintenance of chronic pain. This idea is described in the shared vulnerability model, in which anxiety and pain-related cognition interact in a dysfunctional way, creating "self-perpetuating" distress and functional disability (11). In this study, the group with high levels of pain-related fear in combination with distress (group 4) stood out as having much higher problem levels (e.g. lower acceptance, more healthcare usage, lower quality of life, lower participation rate) and worse outcome compared with the other subgroups, also compared with those with similar levels on 1 of the 2 profiling variables (groups 2 and 3). While there were also significant differences in pain characteristics, these differences were small, and it is unlikely that the high levels of general and specific emotional symptomatology can be explained by the severity of the pain itself. In line with the shared vulnerability model it may be that high levels are rather explained by the (over)activation of emotion regulation strategies, such as worry, rumination, emotional suppression and avoidance behaviours (11). Chronic pain coping difficulties and emotional problems may share cognitive and behavioural mechanisms that function to regulate the emotions evoked by these uncomfortable states. While, in essence, normal and adaptive, regulatory strategies, such as worry and avoidance, can be overly relied on and, paradoxically, lead to worsening of the condition and increased suffering.

The post-treatment results showed that all subgroups improved. This suggests that MMRP is generally effective and, contrary to our initial hypothesis, adds that patients in the subgroup with high levels of emotional distress and pain-related fear improved similarly to patients with other profiles. However, as improvements were generally small, the high score subgroup was still displaying clinical to subclinical post-treatment problem levels. Thus, even though all patients showed similar degrees of improvement, the subgroup with high scores on distress and pain-related fear was still left with problems. It is possible that results could be improved if treatment specifically took into account the emotional comorbidity seen in these patients. This would entail adapting the content of treatment to a treatment that is tailored to fit the profile of the individual patient. Specifically, this could mean tailoring treatments to focus on the ineffective use of emotion regulation strategies, such as excessive worry, rumination and avoidance. This may be an opportunity to treat comorbid problems and thus be more effective for this patient group.

Only approximately one-fifth (21%) of the patients in this study went on to participate in MMRP. These patients were more likely to be female, were younger, and somewhat lower pain intensity than those not continuing to MMRP. Interestingly, it was individuals in subgroup 4 (i.e. those with high pain-related fear and high distress) that were less likely to participate in MMRP. This indicates a differential selection to treatment. One possible explanation is that these patients, perhaps in misdirected problem solving with worry and somatic focus, opt for other directions of care than the training in self-management that MMRP entails. The significantly higher rate of healthcare seeking, and lower willingness to experience pain in this group supports this hypothesis. Another hypothesis is that healthcare staff's fear-avoidance plays a role. Studies show that healthcare providers' fear and avoidance beliefs may influence their treatment practice and guidelines regarding physical and occupational activity (34, 38, 39). However, these hypotheses are untested, and more systematic knowledge is required regarding the basis on which decisions about inclusion in MMRP are made.

This study has some important strengths, but also limitations. The study sample for the cross-sectional part of this study was large and consisted of approximately 70% of consecutive patients with chronic pain referred to 2 major university rehabilitation clinics in 2 different regions in Sweden. While there were differences in pain intensity and interference between our sample and drop-outs, these were very small and therefore unlikely to be of clinical significance. Therefore, a strength of this study is its large and representative sample of patients with chronic pain in a specialist clinical setting. This is also confirmed when comparing pain and interference levels of our sample with other studies

done on patients receiving MMRP (40). A limitation of this study is the substantially smaller sample for the prospective analysis. Twenty-one percent ($n=260$) of the patients in this study continued on to MMRP. While this represents levels of MMRP participation in these 2 clinics, it is unclear how representative this proportion of patients continuing is for other pain clinics. Also, while this sample size is sufficient for analysis of differences between subgroups, there is a need for future studies replicating the specific characteristics of patients continuing and not continuing to MMRP. Also, the lack of outcome information on patients not participating in MMRP influences the conclusions that can be drawn about the specificity of outcome results. For example, it could be that those who did not go on to MMRP had similar outcomes to those of the patients in MMRP. This would mean that the results are not specific to MMRP, but rather the result of, for example, regression to the mean or maturation. However, studies indicate that chronic pain problems do not reduce, and for patients with high levels of fear and distress may even worsen, over time (8). Another limitation is that outcome data was restricted to post-treatment only. It would have been advantageous to include follow-up data, as it remains unclear whether differences seen at post-treatment will be retained, or become larger or smaller with time. However, while 1-year follow-up data is part of the registry data collection procedure, drop-out to follow-up was too large to be able to analyse this follow-up data meaningfully in the current sample.

In conclusion, the results show that 4 groups with different profiles regarding distress and pain-related fear could be meaningfully related to demographic characteristics, pain acceptance, pain interference and quality of life. Prospectively the different profiles related to the selection to, and result of, the MMRP. Specifically, it was individuals with high pain-related fear and high distress who were less likely to participate in MMRP and who had residual problems at clinical levels. These results lend support to psychological theories of pain that stress mechanisms that regulate emotion and other discomforting states of pain, such as the fear avoidance model, the misdirected problem-solving model, and the shared vulnerability model. This study also shows the need for highlighting psychological factors when assessing and treating chronic pain.

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