Outcomes of Interdisciplinary Pain Rehabilitation Across Subgroups of the Multidimensional Pain Inventory – A Study From the Swedish Quality Registry for Pain Rehabilitation

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Abstract

Introduction: The Multidimensional Pain Inventory (MPI) is frequently used in the assessment of chronic pain. Three subgroups have been derived from MPI: adaptive coper (AC), dysfunctional (DYS), and interpersonally distressed (ID). The primary aim of this study was to examine whether outcome of Interdisciplinary Multimodal Pain Rehabilitation Programs (IMMRPs) differed across the MPI subgroups.

Methods: Patients with chronic pain (N = 34,513), included in the Swedish Quality Registry for Pain Rehabilitation, were classified into MPI subgroups and a subset that participated in IMMRPs (N = 13,419) was used to examine overall treatment outcomes using a previously established Multivariate Improvement Score (MIS) and 2 retrospective patient-evaluated benefits from treatment.

Results: The subgroups differed on sociodemographic characteristics, pain duration, and spatial spreading of pain. DYS and ID had the best overall outcomes to MIS. AC had the best outcomes according to the 2 retrospective items. Transition into other subgroups following IMMRP was common and most prominent in DYS and least prominent in AC.

Conclusion: The validity of the MPI subgroups was partially confirmed. DYS and ID had the most severe clinical presentations at baseline and showed most improvement following IMMRP, but overall severity in DYS and ID at post-treatment was still higher than in the AC group. Future studies should examine how processes captured by MPI interact with neurobiological, medical, sociodemographic, and adaptation/coping factors and how these interactions impact severity of chronic pain and treatment outcome.

Key Words: chronic pain, classification, interdisciplinary, multidimensional pain inventory, outcome, pain spreading, rehabilitation, subgroups
The Multidimensional Pain Inventory (MPI) is frequently used in the assessment of chronic pain. A large cohort of chronic pain patients were classified into MPI subgroups and a subset that participated in Interdisciplinary Multimodal Pain Rehabilitation Programs (IMMRPs) was used to examine overall treatment outcomes.

The validity of the MPI subgroups were partially confirmed. Dysfunctional (DYS) and Interpersonally Distressed (ID) subgroups had the most severe clinical presentations at baseline. These subgroups (DYS and ID) showed most improvement following IMMRP, but overall severity in DYS and ID at posttreatment was still higher than in the Adaptive Coper subgroup.

### INTRODUCTION

One fifth of the adult European population suffer from activity-limiting chronic pain of moderate to severe intensity with a duration of at least 6 months. The prevalence of chronic nonmalignant pain is somewhat higher in women than in men and women seek health care more frequently. Chronic pain is influenced by and interacts with physical, psychological, social, and contextual factors and a biopsychosocial framework is often applied to the assessment and management of chronic pain conditions. Moreover, chronic pain severely impacts the daily lives of patients. The clinical presentation of chronic pain, including psychiatric comorbidities (eg, depression, anxiety, insomnia, etc.), is very heterogeneous, even among patients that meet criteria for the same diagnosis according to International Classification of Diseases (ICD). Outcomes of evidence-based interventions for chronic pain are modest and there is a great interest in identifying subgroups of patients with respect to treatment response in order to personalize treatment and improve outcomes.

The Multidimensional Pain Inventory (MPI) is based on a biopsychosocial approach of chronic pain and is commonly used to aid in assessment of patients with chronic pain. MPI and its subscales are sensitive to change in severity of chronic pain and predict sick leave, pain behavior, and future pain. MPI is an established core measure for effectiveness in pain treatment according to the mission of the Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMMPACT). Three subgroups based on psychosocial coping profiles have been derived from the MPI and have replicated in different pain cohorts. The dysfunctional (DYS) subgroup reports high pain severity, marked interference in daily life, high affective distress, low perception of life control, and low levels of activity. The adaptive coper (AC) subgroup is characterized by less severe pain, less interference with activities, less affective distress, and positive perceptions of life control and activity level. The interpersonally distressed (ID) subgroup has been described as perceiving low social support and nonsupporting behaviors from significant others.

Some reports suggest that the DYS and/or ID subgroups have better treatment outcomes than the AC group, whereas other studies have found no significant differences in outcomes among subgroups. A limitation of prior studies is that they have included relatively small samples, lacked evaluations of the clinical importance of differences in outcome across subgroups, or that included samples that poorly represent chronic pain patients seen in clinical practice. Furthermore, the proportions of the different subgroups in clinical practice are unclear and prior studies have reported marked differences in proportions. For example, the proportion classified as AC has ranged from 13% to 44%. Further, to which degree patients transit from one subgroup to another following treatment is insufficiently reported and unclear.

Interdisciplinary Multimodal Pain Rehabilitation Programs (IMMRPs) are well-coordinated complex biopsychosocial interventions. In Sweden, IMMRPs generally have a duration ranging from several weeks to months and are mainly delivered in a group format by an interdisciplinary team. IMMRPs are based on psychological therapies (Cognitive Behavioral Therapy [CBT] and/or Acceptance Commitment Therapy [ACT]) and include group activities, such as pain education, supervised physical activity, and training/activities that promote return to work or education. The goals of IMMRPs are to improve outcomes of importance to patients. However, few studies have investigated real-life outcomes of IMMRPs while considering that changes in many of the outcomes (eg, pain interference,
quality of life, and depression) are highly intercorrelated. Evaluations of complex interventions such as IMMRP should have strategies for handling multiple outcomes. The Swedish Quality Registry for Pain Rehabilitation (SQRP) has 22 mandatory outcome variables for evaluating outcome of IMMRPs. Recently, an overall outcome measure (the Multivariate Improvement Score [MIS]) was computed based on change in the 22 mandatory outcome variables. Furthermore, MIS together with 2 retrospective items that assess to which degree patients have experienced change in pain and in their overall life situation have been applied as composite outcome measures of IMMRPs.

The primary aim of this study was to examine whether patients with chronic pain, subgrouped according to the MPI, had different outcomes on MIS and change in pain and overall life situation following IMMRPs. A secondary aim was to investigate the validity of the MPI classification by examining associations with sociodemographic characteristics and important clinical variables (pain intensity, psychological distress, adaptation/coping, pain cognitions, and health).

**MATERIALS AND METHODS**

The included cohort of patients as well as the variables used in this study have been described in detail in previous publications. Below are brief descriptions of SQRP, the patient cohort, and the variables analyzed in the present study.

**The Swedish Quality Registry for Pain Rehabilitation**

The SQRP receives data from a majority of specialist chronic pain units in Sweden. The registry is based upon patient reported outcome measures (PROMs). PROMs capture a patient’s background, pain intensity, pain-related cognitions, psychological distress, activity/participation in life, and health-related quality of life. Patients complete the questionnaires on up to 3 occasions: (1) before the first visit (baseline) and for those that participate in IMMRP, also (2) immediately after treatment (post-IMMRPs), and (3) at a 12-month follow-up (12-month follow-up). Not all patients participate in IMMRPs due to decisions during assessment (eg, need for further investigation, more reasonable to receive a unimodal treatment, logistic problems related to work or transportation, and unwillingness to participate in the recommended IMMRP).

**Patient cohort**

The patient cohort used in this study was retrieved from SQRP and included patients ≥ 18 years old with complex chronic (≥ 3 months) nonmalignant pain who were referred to specialist care centers between 2008 and 2016. SQRP is a clinical registry and strict criterion for inclusion are not applied. However, general inclusion criteria for IMMRPs are: (a) disabling chronic pain (eg, experiencing major interference in daily life or on long term sick leave); (b) age ≥ 18 years; (c) no further diagnostic assessments and investigations needed; and (d) written consent to participate and attend in IMMRPs. General exclusion criteria for IMMRPs are severe psychiatric comorbidity, abuse of alcohol and/or drugs, diseases that do not allow physical exercise, and specific pain conditions that need other assessments and/or treatments.

The study was conducted in accordance with the Helsinki Declaration and Good Clinical Practice and approved by the Ethical Review Board in Linköping, Sweden (Dnr: 2015/108-31). All participants received written information about the study and gave their written consent.

**Variables**

The variables included in this study are mandatory for the clinical specialist departments registering their data with the SQRP. We extracted the following background data: sex (man/woman); education level (university/upper secondary school/elementary school; this variable was dichotomized and denoted as university vs. no university); and country of birth (Sweden/other Nordic countries [ie, Denmark, Finland, Iceland, and Norway]/Europe except the Nordic countries/outside Europe; this variable was dichotomized and denoted as born in vs. outside of Europe). Number of physician visits due to pain during the last 12 months (categories 0 to 1 time, 2 to 3 times, and ≥ 4 times) were used to indicate amount of health care seeking and the category of ≥ 4 times was used to indicate high health care consumption. Age (years), days with no work or studies and pain duration (days) were also retrieved from the registry. Spatial extent of pain (spreading of pain) was registered using 36 predefined anatomic areas; the number of areas with pain (range = 1 to 36) was summarized and the obtained variable was denoted as Pain Region Index (PRI).
The 22 mandatory baseline and outcome variables in SQRP

There are 22 mandatory outcome variables in SQRP that are registered on up to 3 occasions (baseline, post-IMMRP, and the 12-month follow-up). Detailed reports on the psychometric properties of these variables have been presented in previous publications.8,11,40-42 In the SQRP, predetermined rules are used when handling single missing items of a scale or a subscale; details are reported elsewhere.43 Baseline SQRP variables were used as descriptors of the clinical presentation at baseline together with background variables; several of these variables (as will be indicated) have been presented in a previous study.42

The Multidimensional Pain Inventory. The Swedish version of MPI was used. It has good validity and reliability44 and consists of 3 parts.12,45 Part 1 measures pain severity (Pain severity), pain-related interference (Pain interference), life control (Control), psychological distress (Distress), and perceived social support (Social Support). In part 2, patients report how they perceive that significant others respond to pain or suffering expressed by the patient across 3 domains: punishing responses (Punish), solicitous responses (Protect), and distracting responses (Distract). Part 3 concern participation in various activities, which are combined into a General Activity Index (GAI).44 As reported in the introduction, 3 patterns of psychosocial coping strategies/profiles have been derived from the MPI: AC, DYS, and ID.12 AC is generally characterized by better and DYS by poorer physical and emotional functioning. Perceived lack of support and understanding from significant others characterize ID. Not all patients will be assigned to 1 of these 3 profiles/subgroups and, in agreement with Persson et al., we characterize these patients as belonging to an unclassified group (UC).16 The classification algorithm uses a goodness of fit decision rule to determine whether an individual’s scores are similar to that of a prototypic profile in order to be assigned to AC, ID, or DYS.23 Sociodemographic information, clinical presentation, and outcomes for the AC, DYS, ID, and UC groups will be analyzed in this study.

Pain and health variables. Mean pain intensity during the last 7 days was measured using a 11-graded numerical rating scale (NRS; 0 = no pain to 10 = worst possible pain; NRS = 7 days). Psychological distress was measured with the 2 subscales of the Hospital Anxiety and Depression Scale (HADS) that capture depression (HADS-D) and anxiety (HADS-A).46,47 The Short Form Health Survey (SF-36) was used to assess 8 multidimensional health aspects (graded from 0 to 100 with higher scores indicating a better perception of health).48 The SF-36 scales are: (1) physical functioning, (2) role limitations due to physical functioning, (3) bodily pain, (4) general health, (5) vitality, (6) social functioning, (7) role limitations due to emotional problems, and (8) mental health. Scores across the 8 scales are summarizzed in a physical component summary score (SF-36-PCS) and a mental component summary score (SF-36-MCS). The SF-36-PCS and the SF-36-MCS were used in the present study. The perceived state of health was measured with the European Quality of Life instrument (EQ-5D).19-51 The first part of the instrument presents an index based on 5 dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression (3 alternatives for each dimension). The EQ-5D index is based on representative data from the general population. The second part of EQ-5D is a measure of present health according to a thermometer-like 100-point scale (EQ-VAS) with defined end points (high values indicate good health and low values indicate poor health).

Adaptation/Coping aspects – Pain cognition variables. The abovementioned variables are mandatory in SQRP. We also included optional instruments: the Tampa Scale for Kinesiophobia (TSK) and the 2 subscales from the Chronic Pain Acceptance Questionnaire (CPAQ) – the CPAQ Activity Engagement Scale (CPAQ-AE) and the CPAQ Pain Willingness Scale (CPAQ-PW). Approximately 34% of the patients completed the CPAQ and 43% the TSK. CPAQ measures acceptance in relation to pain and consists of 20 items (rated on a scale from 0 [never true] to 6 [always true]).52,53 CPAQ-AE (score range = 0 to 66) reflects the behavioral component, including pursuit of life activities despite pain. CPAQ-PW (score range = 0 to 54) reflects the attitudinal component of acceptance, including the recognition of the uncontrollability of pain.54 The TSK (score range = 17 to 68) measures fear of movement/reinjury and is a valid assessment tool for chronic pain populations.55-59

Overall outcome measures of IMMRP

Multivariate Improvement Score. Outcome of IMMRPs was measured with the MIS. Most randomized controlled trials (RCTs) of IMMRPs use a
substantial number of outcomes that requires special statistical considerations to deal with multiple comparisons and intercorrelations between outcomes. In a recent large study from SQRP investigating the 22 mandatory outcomes, 18 of the 22 outcomes demonstrated important multivariate intercorrelations according to an advanced principal component analysis. The t-score of the first component (labeled MIS) of the principal component analyses post-IMMRP and at 12-month follow-up represents a comprehensive measure of changes in mainly these 18 outcomes. A detailed description on the computation of MIS has been reported elsewhere. Higher MIS values indicates a larger overall improvement following IMMRP. The following MIS values were obtained for all patients registered in SQRP that participated in IMMRPs during the period of 2008 to 2016: MIS post-IMMRP = mean ± SD = −0.011 ± 2.59, 95% confidence interval [CI] = −0.053 to 0.030, n = 14,666 MIS 12-month follow-up: mean ± SD = −0.011 ± 2.80, 95% CI = −0.069 to 0.048, n = 8851.

Based on MIS, we recently identified 3 subgroups. At the 12-month follow-up, subgroup 1 had the highest MIS (5.01 ± 1.78), subgroup 2 had the second highest MIS (0.78 ± 1.35), and subgroup 3 had the lowest MIS (−2.43 ± 1.39, 95%). A detailed analysis of changes in the 22 mandatory outcome variables showed that subgroup 1 had clear improvements whereas subgroup 3 showed no change or a deterioration. It is important to note that MIS is a relative measure and negative values do not necessarily mean lack of treatment effects.

Changes in pain and life situation following IMMRPs. Both at post-IMMRPs and at the 12-month follow-up, patients rated the amount of positive change in pain (Change-pain) and in the ability to handle life situations in general (Change-life situation) using 5-point Likert scales: Change-pain – markedly increased pain (0) to markedly decreased pain (4) and Change-life situation – markedly worsened (0) to markedly improved (4). Both variables are presented in dichotomized format in the present study (Change-pain: increased pain, no change, and diminished pain; Change-life situation: worsened, no change, and improved).

Statistics

The statistical package IBM SPSS Statistics (version 24.0; IBM Corporation, Somers, NY, USA) was used. A probability of ≤ 0.001 (2-tailed) was accepted as the criteria for statistical significance due to the large number of subjects. In text and tables, we report the mean value ± one standard deviation (±1 SD) of continuous variables and percentages (%) for categorical variables. To compare groups, we used Student’s t-test for independent samples, analysis of variance (ANOVA; Bonferroni post hoc test if significant difference), and Chi square test. For correlation analysis, we used Pearson correlation test and the correlation coefficient (r) and its P value are reported. Effect sizes (ESs; Cohen’s d) for within-group analyses were computed using a calculator when appropriate (https://web power.psychstat.org/models/means01/effectsize.php). Hedges’ g – a measure of effect size weighted according to the relative size of each sample was used for between group ES using a calculator (https://www.socscistatistic s.com/effectsize/default3.aspx). The absolute effect size was considered clinically insignificant for < 0.20, small for 0.20 to 0.49, moderate for 0.50 to 0.79, and large for ≥ 0.80. A detailed statistical description of how MIS was obtained is given elsewhere.

RESULTS

Clinical presentation across the MPI subgroups

As expected, the algorithm for identifying MPI subgroups/profiles identified 3 subgroups, which differed on all MPI variables (Table 1). The algorithm did not classify all subjects and scores for the UC group are also presented in Table 1. At baseline, the DYS subgroup was the largest (39.6%) followed by the ID (21.6%), AC (21.5%), and the UC (17.2%) subgroups. The DYS group reported the worst and the AC group reported the best physical and emotional functioning. The ID subgroup reported high levels of punishment, low levels of protection, and distraction, whereas the AC subgroup reported the lowest levels of punishment and distraction. According to parts 1 and 2 of the MPI, the UC subgroup was an intermediary between the AC and ID subgroups. When comparing all 4 groups, significant differences were present for all variables except for MPI-GAI (see Table 1). ESs for AC vs. DYS comparisons were large or very large with the exception of moderate ESs for MPI-punish and MPI-GAI (see Table 1).

A comparison of the MPI subgroups on non-MPI variables revealed significant differences on all variables (Table 2). According to the categorical variables, ID had the highest proportion of women (77.7%) whereas the
lowest proportion was found in AC (69.4%). The DYS group had the highest proportion of patients born outside of Europe, the lowest proportion with university education, and the highest proportion characterized by high health care consumption. According to the continuous variables, the AC group generally reported the least severe clinical presentation followed by the UC, ID, and DYS groups. The same pattern was found for health-related variables (EQ variables and SF-36 indices) and the adaptation/coping variables (CPAQ and TSK). Exceptions from this pattern were that ID had most days with no work/studies and the longest duration of pain. The pairwise comparisons of AC vs. DYS showed at least large ESs for pain intensity, both subscales of HADS, both measures of EQ and SF-36-MCS, and the 3 adaptation/coping variables (CPAQ-AE and CPAQ-PW and TSK; see Table 2), whereas a moderate ES was noted for SF-36-PCS. Pain duration and PRI were associated with small ESs and comparisons for age and days with no work/studies indicated insignificant ESs (see Table 2).

**Participation in and general outcomes of IMMRP**

The participation rate in IMMRP differed significantly across subgroups with the highest participation in the UC group and the lowest in the DYS group (Table 3). The DYS group followed by the ID group had the best outcomes according to MIS at both post-IMMRP and at the 12-month follow-up. The AC group showed the smallest improvements according to MIS (see Table 3) and the UC group was intermediary between AC and ID. The pairwise ESs of MIS for AC vs. ID and DYS were small (see Table 3). When scrutinizing the individual outcome variables – as expected from the MIS results – the pre-post IMMRP ESs differed across subgroups. Hence, in the AC group, changes from baseline to post-IMMRP were small or clinically insignificant (Table 4), whereas 9 of the 19 variables in the DYS group showed changes with at least a moderate ES. Corresponding figures in the ID and UC groups were 8 and 1, respectively. At the 12-month follow-up, all within-subgroup ESs in the AC subgroup (except for SF-36-PCS and the CPAQ variables, moderate ESs) were small or clinically insignificant (Table 5). Nine of the variables in the DYS subgroup were associated with at least a moderate ES and the rest (except MPI-punish) showed small ESs. Corresponding results for the ID subgroup were 9 variables with a moderate ES and 3 with a clinically insignificant ES. In the UC subgroup, 5 variables showed a moderate ES, 11 variables showed a small ES, and 3 variables had a clinically insignificant ES.

Contrary to the findings for MIS, the retrospective item concerning patients’ self-evaluation of change in pain showed the highest proportion of improvement in AC at both post-IMMRP and at the 12-month follow-up. The differences across the subgroups were small but

### TABLE 1. The Input Variables From MPI Used to Derive the 3 Clusters of MPI (AC, ID, and DYS)

| Subgroups | AC Mean | n = 7 427 | SD | ID Mean | n = 7 469 | SD | DYS Mean | n = 13 683 | SD | Statistics 3 Groups P Value | Post Hoc | UC Mean | n = 5 934 | SD | Statistics 4 Groups P Value | Post Hoc | ES AC vs. DYS |
|-----------|---------|-----------|----|---------|-----------|----|----------|-----------|----|---------------------------|----------|----------|-----------|----|---------------------------|----------|-------------|
| Pain severity | 3.7 | 1.0 | 4.5 | 0.9 | 5.0 | 0.7 | ≤ 0.001 | All different | 4.3 | 0.8 | < 0.001 | All different | 1.59 |
| Pain interference Control | 3.3 | 1.0 | 4.6 | 0.9 | 5.0 | 0.7 | ≤ 0.001 | All different | 4.3 | 0.9 | < 0.001 | All different | 2.08 |
| Distress | 3.6 | 0.9 | 2.4 | 1.0 | 2.2 | 1.1 | < 0.001 | All different | 2.9 | 1.0 | < 0.001 | All different | 1.35 |
| Social support | 2.0 | 1.0 | 4.0 | 1.0 | 4.2 | 1.0 | < 0.001 | All different | 3.3 | 1.0 | < 0.001 | All different | 2.20 |
| Punish | 4.3 | 1.0 | 2.5 | 1.1 | 5.2 | 0.7 | < 0.001 | All different | 4.2 | 1.0 | < 0.001 | All different | 1.10 |
| Protect | 1.0 | 0.9 | 2.9 | 1.5 | 1.6 | 1.3 | < 0.001 | All different | 1.7 | 1.2 | < 0.001 | All different | 0.51 |
| Distract | 2.7 | 1.2 | 1.6 | 1.0 | 4.1 | 1.1 | < 0.001 | All different | 2.8 | 1.1 | < 0.001 | All different | 1.23 |
| GAI | 2.2 | 1.1 | 1.6 | 1.0 | 3.4 | 1.0 | < 0.001 | All different | 2.4 | 1.0 | < 0.001 | All different | 1.16 |
| Note: For comparison is also added those not classified (UC). Statistics 3 groups compare the 3 subgroups (AC, ID, and DYS) and Statistics 4 groups also include the UC group. Furrthest to the right effect size (ES; Hedges g) for AC vs. DYS. ES was considered clinically insignificant for < 0.20, small for 0.20 to 0.49, moderate for 0.50 to 0.79, large for 0.80 to 1.29, and very large for > 1.3. AC, adaptive copers; ID, interpersonally distressed patients; DYS, patients with dysfunctional profile; UC, unclassified; GAI, General Activity Index; MPI, Multidimensional Pain Inventory; ES, effect size.
TABLE 2. Sociodemographic and Other Variables Across the 3 MPI Clusters for Variables not Used for Classification

| Subgroups | AC | ID | DYS | UC | Statistics | ES | Comment |
|-----------|----|----|-----|----|------------|----|---------|
| **Women** | 69.4 | 77.7 | 72.1 | 74.0 | < 0.001 | 140.2; 3 | |
| **Born outside Europe** | 4.8 | 9.4 | 20.8 | 9.0 | < 0.001 | 1345.1; 3 | |
| **University education** | 29.8 | 25.7 | 19.0 | 25.9 | < 0.001 | 339.3; 3 | |
| **High health care (< 4 doctor visits)** | 56.0 | 68.2 | 80.9 | 67.1 | < 0.001 | 1560.1; 6 | |
| **Age (years)** | Mean SD | Mean SD | Mean SD | Mean SD | P Value | Post hoc | |
| 43.8 | 12.0 | 43.3 | 10.3 | 42.1 | 11.3 | 42.9 | 11.5 | < 0.001 | ID – UC; other different | 0.15 | |
| **Days with no work/studies** | 1225 | 2249 | 1486 | 2450 | 1275 | 2213 | 1295 | 2588 | < 0.001 | AC – DYS; UC; DYS – UC; | 0.11 | AC vs. ID |
| **Pain intensity (days)** | 2969 | 3349 | 3574 | 3574 | 3116 | 3205 | 3116 | 3205 | < 0.001 | DYS – ID, other different | 0.47 | |
| **NRS – 7 days** | 5.9 | 1.8 | 7.0 | 1.6 | 7.8 | 1.4 | 6.7 | 1.6 | < 0.001 | All different | 1.22 | |
| **HADS-D** | 4.6 | 3.3 | 10.3 | 4.2 | 10.2 | 4.4 | 7.9 | 4.0 | < 0.001 | DYS – ID, other different | 1.38 | |
| **HADS-A** | 5.1 | 3.5 | 10.5 | 4.5 | 11.1 | 4.7 | 8.3 | 4.3 | < 0.001 | All different | 1.39 | |
| **EQ-SD Index** | 0.46 | 0.29 | 0.23 | 0.30 | 0.10 | 0.26 | 0.29 | 0.30 | < 0.001 | All different | 1.33 | |
| **EQ-VAS** | 53.1 | 18.9 | 38.8 | 18.5 | 33.8 | 19.1 | 42.7 | 18.3 | < 0.001 | All different | 1.01 | |
| **SF-36-PCS** | 31.3 | 9.2 | 29.6 | 7.8 | 26.4 | 7.2 | 28.9 | 8.0 | < 0.001 | All different | 1.62 | |
| **SF-36-MCS** | 47.1 | 10.9 | 30.8 | 11.6 | 31.1 | 11.7 | 37.5 | 12.1 | < 0.001 | DYS – ID, other different | 1.45 | AC vs. ID |
| **CPAQ-AE** | 34.6 | 10.7 | 25.2 | 11.2 | 20.9 | 11.4 | 27.7 | 10.8 | < 0.001 | All different | 1.23 | |
| **CPAQ-PW** | 27.0 | 8.3 | 21.7 | 8.3 | 18.6 | 8.4 | 22.6 | 8.0 | < 0.001 | All different | 1.00 | |
| **TSK** | 34.5 | 7.9 | 39.3 | 8.8 | 42.6 | 9.3 | 38.1 | 8.2 | < 0.001 | All different | 0.92 | |

Note: To the right is shown statistics and effect sizes (ES; Hedges g). ES were computed between the subgroups with most extreme values (ie, generally AC vs. DYS if not otherwise stated). ES was considered clinically insignificant for < 0.20, small for 0.20 to 0.49, moderate for 0.50 to 0.79, large for 0.80 to 1.29, and very large for ≥ 1.3.

AC, Adaptive copers; ID, interpersonally distressed patients; DYS, patients with dysfunctional profile; UC, unclassified patients; PRI, Pain Region Index; NRS = 7 days, the pain intensity as measured by a numeric rating scale for the previous 7 days; HADS, Hospital Anxiety and Depression Scale; HADS-D, depression subscale of HADS; HADS-A, anxiety subscale of HADS; EQ-SD-index, the index of the European quality of life instrument; EQ-VAS, the European quality of life instrument thermometer-like scale; SF-36-PCS, physical component summary score of SF-36; SF-36-MCS, mental component summary score of SF-36; CPAQ, Chronic Pain Acceptance Questionnaire; CPAQ-AE, the Activity Engagement Scale of CPAQ; CPAQ-PW, the Pain Willingness Scale of CPAQ; TSK, the Tampa Scale for Kinesiophobia; MPI, Multidimensional Pain Inventory; ES, effect size; df, degree of freedom.

significant (see Table 3). A similar pattern was observed regarding change in life situation, again with small differences.

When analyzing subgroup classification after IMMRP (Figure 1), > 70% of patients included in the AC group at baseline were still classified as AC at post-IMMRP and at the 12-month follow-up. For DYS, 45% to 50% remained in the DYS subgroup whereas 25% to 27% transitioned to the AC subgroup immediately after IMMRP and at the 12-month follow-up. For ID, 57% to 59% remained in the ID group at post-IMMRP and at the 12-month follow-up whereas 19% to 22% moved to the AC subgroup (see Figure 1). Only 22% to 23% remained in the UC subgroup after IMMRP with the largest proportion transitioning to the AC (44% at both time points) followed by the ID (17% to 20%) subgroup.

DISCUSSION

Major results

Major results were that most patients were classified as DYS followed by ID, AC, and UC. The subgroups were validated in relation to variables not included in the MPI algorithm (ie, pain intensity, psychological distress, adaptation/coping, and overall health); AC reported least and DYS most severity and impairment. Moreover, the proportion of patients born outside of Europe, with no university education and large health care consumption, was highest in DYS. The most common subgroup to participate in IMMRP was the UC group and the lowest participation rate was found in the DYS group. According to MIS and pre-post change in separate variables, the DYS and ID groups showed most improvement following IMMRP and least improvement was found in the AC group, but ESs were in the small range. The 2 retrospective items indicated most improvement in the AC group, but differences were small. Transition from one subgroup to another following IMMRP was common and most prominent in UC, followed by DYS, ID, and AC. The proportion transitioning to AC was highest in UC (44% at both time points) followed by DYS (25% to 27%) and ID (19% to 22%).

Size and validity of MPI subgroups

In this large cohort of patients from specialist clinical departments, DYS was most prevalent followed by ID,
AC, and UC. Proportions of patients in each subgroup have differed considerably in previous studies, which may be due to sample characteristics and level of care (eg, primary, secondary, and tertiary). The prevalence of the MPI subgroups in the general population or in primary care is largely unknown; however, in a small primary care study of patients with low back (n = 88), AC was the largest subgroup (44%) and DYS the smallest (22%). This suggests that there may be a selection of DYS and ID patients referred to specialist clinical departments.

The validity of the MPI classification has been questioned, but, in the present study, the validity of the subgroups was confirmed in relation to variables not included in the MPI algorithm and similar results have previously been reported for life satisfaction. In agreement with the original article, AC had the least severe clinical presentation followed by UC, ID, and with DYS having the most severe clinical presentation. Our results also agree with cluster analyses using psychological variables as input, which show that clusters with prominent psychological burden (ie, DYS and ID) have higher pain intensity/severity.

Individuals classified as AC were originally labeled as minimizers/adaptive copers. Turk and Rudy suggested that people in this subgroup may deny or minimize the extent and impact of their pain problems. Of note, Turk and Rudy did not suggest that ID and DYS may have exaggerated their problems. The term “adaptive coper” (AC) implies that these patients cope with their pain more constructively and thereby have less severe pain intensity and interference than patients in the ID and DYS groups. However, such causal claims are not justified, as higher pain intensity may result in coping strategies more in line with what is described in ID and DYS. Moreover, the choice of the term adaptive coper was not grounded in investigations of coping strategies in the subgroups. Studies from different pain cohorts report that DYS has a high degree of catastrophizing, but it is unclear whether AC or ID have the lowest degree of catastrophizing; a similar pattern has been shown for behavioral coping strategies. The pain cognition variables TSK and CPAQ, reflecting facets of adaptation and coping that are targets for CBT (eg, ACT and pain education, indicated that the AC group had the best functioning followed by UC, ID, and with the worst functioning in DYS). This supports the suggestions made by Turk and colleagues.

In previous studies, results were found that DYS patients were more likely to be unemployed. Turk and Rudy also investigated if sex, age, or pain duration explained cluster differences because the clusters

### TABLE 3. Participation Rate in IMMRP, and Overall Outcomes of IMMRP (MIS, Change in Pain and Change in Life Situation) Post-IMMRP and at 12-Month Follow-Up

| Subgroups | AC | ID | DYS | UC | Statistics | Chi Square; df | ES |
|-----------|----|----|-----|----|------------|----------------|----|
| Participation rate (%) | | | | | | | |
| Mean | SD | n | Mean | SD | n | Mean | SD | n | Mean | SD | n | | | |
| MIS post | | | | | | | | | | | | | | |
| MIS 12-month FU | | | | | | | | | | | | | | |
| Improved in: % | | | | | | | | | | | | | | |
| Change pain post | | | | | | | | | | | | | | |
| Change pain 12-month FU | | | | | | | | | | | | | | |
| Change life post | | | | | | | | | | | | | | |
| change life 12-month FU | | | | | | | | | | | | | | |

Note: To the right is shown statistics and effect sizes (ES; Hedges g). ES was considered clinically insignificant for <0.20, small for 0.20–0.49, moderate for 0.50–0.79, large for 0.80–1.29, and very large for ≥1.3.

AC, Adaptive copers; ID, interpersonally distressed patients; DYS, patients with dysfunctional profile; UC, unclassified patients; IMMRP, Interdisciplinary Multimodal Pain Rehabilitation Program; MIS, Multidimensional Pain Inventory; df, degree of freedom; FU, follow up.
| Subgroups | N = 2469 | N = 2778 | N = 4875 | N = 2282 |
|-----------|----------|----------|----------|----------|
|           | Pre/post | Pre/post | Pre/post | Pre/post |
| Variables | Mean ± SD | Mean ± SD | Mean ± SD | Mean ± SD |
| NRS-7 days | 5.8 ± 1.8 | 5.1 ± 2.2 | < 0.001 | 0.32 | 6.8 ± 1.6 | 5.9 ± 2.0 | < 0.001 | 0.44 | 7.6 ± 1.4 | 6.5 ± 1.9 | < 0.001 | 0.54 | 6.7 ± 1.6 | 5.8 ± 2.0 | < 0.001 | 0.44 |
| HADS-D | 5.3 ± 3.5 | 4.9 ± 3.5 | < 0.001 | 0.12 | 10.4 ± 4.4 | 8.7 ± 4.3 | < 0.001 | 0.41 | 10.6 ± 4.5 | 9.0 ± 4.6 | < 0.001 | 0.39 | 8.2 ± 4.1 | 7.2 ± 4.1 | < 0.001 | 0.30 |
| Pain severity | 4.9 ± 3.2 | 4.1 ± 3.2 | < 0.001 | 0.23 | 10.1 ± 4.1 | 7.7 ± 4.2 | < 0.001 | 0.60 | 9.7 ± 4.2 | 7.6 ± 4.4 | < 0.001 | 0.53 | 8.0 ± 3.9 | 6.3 ± 3.9 | < 0.001 | 0.48 |
| EQ-5D Index | 3.6 ± 0.9 | 3.2 ± 1.2 | < 0.001 | 0.38 | 4.4 ± 0.8 | 3.9 ± 1.1 | < 0.001 | 0.52 | 4.9 ± 0.7 | 4.3 ± 1.0 | < 0.001 | 0.65 | 4.3 ± 0.8 | 3.8 ± 1.1 | < 0.001 | 0.49 |
| EQ-VAS | 3.3 ± 1.0 | 3.1 ± 1.2 | < 0.001 | 0.28 | 4.6 ± 0.8 | 4.1 ± 1.1 | < 0.001 | 0.56 | 4.9 ± 0.7 | 4.4 ± 1.0 | < 0.001 | 0.59 | 4.3 ± 0.8 | 3.9 ± 1.1 | < 0.001 | 0.46 |

Note: Within subgroup statistics and within subgroup effect sizes are reported. AC, Adaptive coping; ID, interpersonally distressed patients; DYS, patients with a dysfunctional profile; UC, unclassified patients; ES, effect size; ES was considered clinically insignificant for < 0.20, small for 0.20 to 0.49, moderate for 0.50 to 0.79, large for 0.80 to 1.29, and very large for ≥ 1.3. Note the lower number of subjects for CPAQ-AE (AC = 702, ID = 1006, DYS = 1608, and UC = 794), CPAQ-PW (AC = 744, ID = 1054, DYS = 1726, and UC = 884) and TSK (AC = 961, ID = 1243, DYS = 2036, and UC = 1038). NRS-7 days, pain intensity as assessed by a numeric rating scale for the previous 7 days; HADS, Hospital Anxiety and Depression Scale; HADS-D, depression subscale of HADS; HADS-A, anxiety subscale of HADS; EQ-SD-index, the index of the European quality of life instrument; EQ-VAS, the European quality of life instrument thermometer-like scale; SF-36, the Short Form 36 Health Survey; SF-36-PCS, physical component summary score of SF-36; SF-36-MCS, mental component summary score of SF-36; CPAQ, Chronic Pain Acceptance Questionnaire; CPAQ-AE, the Activity Engagement Scale of CPAQ; CPAQ-PW, the Pain Will Ingress Scale of CPAQ; TSK, The Tampa Scale for Kinesiophobia (GAI, General Activity Index; IMMRP, Interdisciplinary Multimodal Pain Rehabilitation Program).
| Subgroups | N = 1709 | N = 1622 | N = 2617 | N = 1386 |
|-----------|----------|----------|----------|----------|
|           | to 1847  | to 1800  | to 2953  | to 1552  |
| Variables | Mean ± SD | Mean ± SD | Mean ± SD | Mean ± SD |
| NRS-7 days | 5.8 ± 1.8 | 4.8 ± 2.4 | 5.8 ± 2.2 | 5.8 ± 2.1 |
| HADS-A | 5.2 ± 3.4 | 5.2 ± 3.7 | 5.2 ± 4.2 | 5.2 ± 3.7 |
| HADS-D | 4.7 ± 3.1 | 4.2 ± 3.6 | 4.2 ± 4.6 | 4.2 ± 4.0 |
| Pain severity | 3.7 ± 0.9 | 3.2 ± 1.3 | 3.2 ± 1.4 | 3.2 ± 1.3 |
| Pain interference | 3.9 ± 1.3 | 3.1 ± 1.2 | 3.1 ± 1.2 | 3.1 ± 1.2 |
| Control | 3.5 ± 1.1 | 3.8 ± 1.2 | 3.8 ± 1.2 | 3.8 ± 1.2 |
| Distress | 2.7 ± 1.0 | 2.5 ± 1.2 | 2.5 ± 1.2 | 2.5 ± 1.2 |
| Social support | 4.3 ± 0.9 | 4.3 ± 1.0 | 4.3 ± 1.0 | 4.3 ± 1.0 |
| Punish | 3.0 ± 1.0 | 3.2 ± 1.1 | 3.2 ± 1.1 | 3.2 ± 1.1 |
| Protect | 2.7 ± 1.0 | 2.3 ± 1.2 | 2.3 ± 1.2 | 2.3 ± 1.2 |
| Distact | 2.2 ± 1.1 | 2.2 ± 1.3 | 2.2 ± 1.3 | 2.2 ± 1.3 |
| GAI | 2.7 ± 0.7 | 2.8 ± 0.8 | 2.8 ± 0.8 | 2.8 ± 0.8 |
| EQ-SI index | 0.5 ± 0.3 | 0.6 ± 0.3 | 0.6 ± 0.3 | 0.6 ± 0.3 |
| EQ-VAS | 53.1 ± 17.9 | 62.2 ± 21.7 | 53.1 ± 17.9 | 62.2 ± 21.7 |
| SF-36-PCS | 31.3 ± 8.5 | 36.4 ± 10.8 | 31.3 ± 8.5 | 36.4 ± 10.8 |
| SF-36-MCS | 47.2 ± 10.6 | 47.0 ± 11.6 | 47.2 ± 10.6 | 47.0 ± 11.6 |
| CPAQ-AE | 33.9 ± 10.3 | 39.5 ± 11.4 | 33.9 ± 10.3 | 39.5 ± 11.4 |
| CPAQ-PW | 26.5 ± 8.4 | 30.8 ± 8.7 | 26.5 ± 8.4 | 30.8 ± 8.7 |
| TSK | 34.0 ± 7.7 | 31.0 ± 7.9 | 34.0 ± 7.7 | 31.0 ± 7.9 |

Note: Within subgroup statistics and within subgroup effect sizes are reported. AC, Adaptive coping; ID, interpersonally distressed patients; DYS, patients with dysfunctional profile; UC, unclassified patients; 12 month FU, 12-month follow-up; ES, effect size; ES was considered clinically insignificant for < 0.20, small for 0.20 to 0.49, moderate for 0.50 to 0.79, large for 0.80 to 1.29, and very large for ≥ 1.3. Note the lower number of subjects for CPAQ-AE (AC = 481, ID = 640, DYS = 1032, and UC = 513), CPAQ-PW (AC = 507, ID = 661, DYS = 1095, and UC = 538), and TSK (AC = 628, ID = 736, DYS = 1230, and UC = 634); NRS-7 days, pain intensity as measured by a numeric rating scale for the previous 7 days; HADS, Hospital Anxiety and Depression Scale; HADS-D, depression subscale of HADS; HADS-A, anxiety subscale of HADS; EQ-SI-index, the index of the European quality of life instrument; EQ-VAS, the European quality of life instrument thermometer-like scale; SF-36, the Short Form 36 Health Survey; SF-36-PCS, physical component summary score of SF-36; SF-36-MCS, mental component summary score of SF-36; CPAQ, Chronic Pain Acceptance Questionnaire; CPAQ-AE, the Activity Engagement Scale of CPAQ; CPAQ-PW, the Pain Willingness Scale of CPAQ; TSK, The Tampa Scale for Kinesiophobia; GAI, General Activity Index; IMMARP, Interdisciplinary Multimodal Pain Rehabilitation Program.
would be of little incremental utility if basic patient characteristics explained cluster differences. They found no such significant differences. This was not the case in the present study where more than 20% of the DYS patients (ie, the subgroup with the worst clinical situation) were born outside of Europe compared to 5% in AC (the subgroup with the least severe clinical presentation). The highest proportion with university education was found in the AC group (30%) and the lowest in the DYS group (19%), again suggesting important sociodemographic differences across subgroups. Recently, an SQRP study showed that clusters based on the combination of sex, country of birth, and education level were associated with prominent differences in clinical presentation when comparing the 2 most extreme clusters. It may be that a lower education level reflects occupational conditions with higher risk for developing and maintaining pain conditions and a tendency to apply less effective individual pain approaches. In addition, country of birth and sex have been shown to influence chronic pain and its consequences. MPI does not cover these sociodemographic factors and there is a risk that such factors are not considered if interventions and treatments are designed solely on MPI profiles. Of note, sociodemographic variables contribute relatively little to the total variation in clinical presentation, but they may still be important for individual patients classified as DYS or ID.

No relationships have been established between common clinical signs (eg, lumbar flexion, cervical range of motion, Lasègue sign, etc.) and MPI subgroups, and Turk suggested that MPI classifications (considered as psychosocial classifications) and medical classifications were truly independent. Conceptually – especially in the context of a biopsychosocial model of pain – it may not be justified to expect that medical aspects are unrelated to psychosocial aspects of pain; pain intensity aspects – a common sign in many conditions – are in fact involved in several of the scales.
of MPI (eg, pain severity and pain interference). In the present study, we could show that DYS and ID had more widespread pain than UC and AC. This indicates that a higher proportion of nociplastic pain conditions (eg, chronic widespread pain and fibromyalgia) are present in ID and DYS patients. Chronic widespread pain is associated with a more severe clinical presentation, including a longer duration of pain.69-73 Chronic widespread pain is also more frequent in women, individuals born outside of Europe, and those with a lower education level.2,38,74-79 Furthermore, cardiovascular diseases and diabetes are more prevalent in patients with widespread pain, which contribute to the total burden of disease for patients.73,78,80 Future research should investigate if the MPI subgroups have different proportions of ICD pain diagnoses and pain mechanisms (nociceptive, neuropathic, or nociplastic). Such information is not directly reflected in the MPI classification but should be considered in clinical care, as spreading of pain and comorbidities may be etiological and influence treatment design and success.

**Participation rate**

Participation in IMMRP was lowest in the DYS group and, even though differences across MPI subgroups were not large, this result is in line with other studies from SQRP. That is, patients with the most severe clinical presentation participate in IMMRP to a lower extent than those with a less severe clinical presentation.8,38,67 Unfortunately, no detailed information exists about reasons for participation or nonparticipation in IMMRP in SQRP. Hence, nonparticipation can reflect choices and attitudes of the team/clinicians but also decisions, perceptions, and circumstances among patients.38,62,67

**Who benefits most from IMMRP?**

Systematic reviews (SRs) conclude that IMMRP is an effective intervention with small to moderate effects for patients with chronic pain.33,81,82 However, RCTs – constituting the foundation of SRs – do not necessarily reflect real-life clinical practice and hence an intervention must show effectiveness under clinically relevant conditions.83,84 Recent SQRP studies indicate that effects are not independent of clinical presentation at baseline.7,8,67,69 The present results partially challenge a general conclusion that treatments based on subgrouping at baseline have limited success.85 However, hitherto attempts to design special rehabilitation interventions for the MPI subgroups have not produced better results than standard care.86 The pattern that patients with the most severe clinical picture (ie, DYS and ID) generally benefit most from IMMRP agrees with studies from SQRP8,67 and other studies.14,17,19-22,87 Further, the present study contrasts with considerably smaller studies reporting that subgroups of MPI do not display different outcomes or predict outcome after rehabilitation interventions.15,22,27 Psychological distress, however, has been associated with worse treatment outcomes.88-91 The fact that ID and DYS (characterized by relatively prominent psychological distress) had larger improvements for MIS and for most of the individual variables may seem unexpected, but it is important to recognize that IMMRPs are based upon and include CBT/ACT interventions and thus may be particularly suited to produce improvements in psychological distress.

MIS is a relative measure, which reflects changes in most of the mandatory outcome variables in SQRP. The small differences for MIS across MPI subgroups should be seen in the perspective that patients who receive pain rehabilitation in specialist clinical departments frequently (and according to guidelines) have tried other treatments with no or little effect. ID showed better MIS results than AC and UC in this study, which is important because earlier reports have been conflicting whether ID report significant improvements after rehabilitation interventions.17,19,21,26,30,87

When scrutinizing the within-group changes for the individual variables, most variables in all subgroups at both post-treatment and at the 12-month follow-up showed significant improvements. Improvements for pain intensity aspects (NRS = 7 days and MPI pain severity) were also noted across the 3 MPI subgroups, which contrasts some SRs that report no evidence for efficacy with respect to pain intensity. Patients with pain consider reduction of pain intensity to be the most important outcome.92 However, as discussed elsewhere, reduction of pain intensity as a primary goal of pain treatment is complicated for several reasons and Swedish IMMRPs have adopted acceptance as a cornerstone of the CBT component of IMMRP where patients are advised against establishing pain intensity reduction goals.7 However, ethical questions arise if clinical practice ignores research and wishes of the patients. There is a need to address the complexity of pain intensity in IMMRPs and not underestimate the patients’ ability to grasp, once explained, the complexity of pain experiences. Patients should be informed about
the effects that are seen in pain reduction at a group level and at the same time be made aware of how aiming for pain reduction as a primary goal can be a roadblock for change. Such an incorporation can improve motivation for IMMRP components (eg, pain education, physical exercise, and psychological intervention).

Significant positive changes occurred in AC for most variables even though the within-group ESs generally were small or clinically insignificant whereas DYS and ID frequently displayed moderate ESs. Less improvement in AC – both for MIS and individual variables – can be explained by that they have less room for improvement or that treatment in fact is less effective for this group.\textsuperscript{20} Even though this study showed generally small or clinically unimportant significant improvements in AC, the small improvements may have been of value for the AC patients, as indicated by quite substantial changes in 3 quality-of-life variables, adaptive/coping variables (CPAQ and TSK) and the 2 retrospective items. Notably, the TSK, representing fear of movement and, as such, an important target for treatment, reached an ES of 0.49 in the AC group post-IMMRP and both CPAQ variables had moderate ESs at the 12-month follow-up. Moreover, at both time points, AC showed the highest proportions with improved pain and improved life situation according to the change in pain and change in life situation variables. These improvements may partially be due to improvements in factors not measured in SQRP. Taken together, IMMRPs appear to be of value also for AC patients, but future research should aim to make IMMRPs equally effective in this subgroup of patients as in the other MPI subgroups.

This study as well as other studies using the MPI classification points toward the need to develop different interventions for different clusters or subgroups of patients. The most comprehensive and expensive resources should be offered to patients with the most complicated or severe clinical presentation (ie, DYS and ID). Bergström et al. suggested that ID and DYS patients may benefit from combination treatments that include psychosocial components, whereas AC patients may respond better to unidimensional interventions without a psychosocial component.\textsuperscript{24} Turk stated that AC treatment ought to include psychological treatment because some AC patients may be minimizers.\textsuperscript{13} Moreover, Turk considered reassurance, maintenance, and relapse prevention as important components for AC, whereas some CBT components may be less useful.\textsuperscript{13} It is possible that patients belonging to the AC subgroup would be good candidates for primary care-based multimodal interventions and/or internet-based interventions; neither of these exclude psychosocial interventions. However, the patients in the AC subgroup in the present study had been referred to specialist clinical departments, which makes it likely that interventions in primary care had not been sufficient. Speculatively, some of the AC patients may be in the process of transitioning to DYS or ID, which is an argument for keeping these highly selected AC patients in specialized units.

Approximately 50% of DYS patients and around 40% of ID patients transitioned to other clusters following IMMRP. These transitions are largely in line with the MIS results and indicate positive change, even though some of the transitions may reflect instability in the MPI classification.\textsuperscript{28,93-95} However, a quite large proportion remained in their original cluster, which either indicates that MPI to some extent is insensitive to clinical valuable change and/or that IMMRP is not optimal for all participants. In favor of the latter, is the finding that the DYS and ID groups reported considerable burden and a worse situation compared to AC at both post-treatment and at the 12-month follow-up. For instance, pain intensity (NRS = 7 days) was above 5 at the group level in all subgroups (except in AC group at the 12-month follow-up). Furthermore, pain intensity at post-IMMRP and at the 12-month follow-up was higher in the DYS group than in the AC group before treatment. Hence, it could be questioned whether IMMRPs and its components are optimal because pain intensity, pain interference, and psychological distress after IMMRP are still very elevated for many participants. For instance, the activated nociceptive and pain mechanisms (eg, central nervous system alterations, central and peripheral sensitization mechanisms, altered descending control, and comprehensive alterations in peripheral tissues) may not be sufficiently influenced. In fact, clinically applicable measures of these neurobiological aspects are to a large extent lacking.

The literature reflects great interest in identifying subgroups (clusters) of patients and investigating how these clusters benefit from treatment. For low back pain, such clusters have been based on genetics, pathoanatomy, psychological and psychosocial variables, activity-related behavioral approaches, or patterns of signs and symptoms.\textsuperscript{9,6,2,63,96-99} Most of these studies have been hypothesis driven with respect to the input variables used, whereas others have been used objective methods to select input variables from a larger set of variables. In
some studies, a specific diagnosis has been investigated, whereas in other studies several chronic pain diagnoses have been represented. Moreover, different methods have been used for the identification of subgroups (clusters; eg, advanced principal component analysis, cluster analysis, and latent class analysis). To the best of our knowledge, there is no review that has compared MPI with other classification methods with respect to treatment outcomes. However, MPI was stable compared to 2 other classification systems for low back pain. Using the present cohort of patients from SQRP, we have published other subgrouping studies. Hence, when subgrouping patients using based upon sex, education level, and country of birth, we identified 5 subgroups and the most prominent effect sizes for MIS between clusters at 12-month follow-up were 0.21 to 0.23. When using the spatial pain extent on the body (spreading of pain) and comparing the 2 extremes we found an effect size of 0.23 for MIS at the same time point. The present study found somewhat higher effect sizes (0.28 to 0.31) at the 12-month follow-up, but these are still considered as small. Generally, treatments based on subgrouping only have had small to moderate effects. The studies based on this large pain cohort from SQRP do not deviate from this conclusion. In future studies of IMMRP, comparisons between MPI and other established classification systems are desirable. Such comparisons need to include pros and cons from a patient perspective and whether the systems are appropriate in primary care.

**Strengths and Limitations**

The large nationwide cohort of patients with chronic pain in real-life settings is a strength of the present study. However, there is also a need for large studies from primary care and the general population. We used ESs to determine if statistically significant differences were clinically important, which is a strength with respect to clinical interpretation. Well-known PROM variables were used but repeated assessments may be problematic. A biopsychosocial approach was used when selecting the mandatory PROM outcomes, and MIS extracts the most important global information from changes in these outcomes, which is a strength. Of note, regression to the mean is not likely to explain the larger improvements in the subgroups (eg, ID and DYS) with the largest improvements, as reported in another SQRP study. Although all specialist clinics adhere to the general description of IMMRP, there may be heterogeneity regarding scope and intensity of the different components as well as competence differences among therapists. Individual differences in adherence to IMMRP may also exist across MPI profiles. Data for an 8-year period (2008 to 2016) were used and changes in the content of IMMRP may have occurred, but no detailed information is available that captures these aspects, which is a limitation.

**CONCLUSIONS**

The validity of the subgroups of MPI was partially confirmed in this large study of patients from everyday clinical practice. However, differences in sociodemographic variables as well as in pain duration and widespread pain were found across the MPI subgroups. The DYS and ID subgroups had the most severe clinical presentation at baseline and showed the largest improvement following IMMRP. The AC group had the least severe clinical presentation at baseline and showed least improvement following IMMRP, but severity at the post-treatment and 12-month follow-up assessments were still lower in this subgroup compared to the DYS and ID subgroups. Future studies should examine how processes captured by MPI interact with neurobiological, medical, sociodemographic, and adaptation/coping factors and how these interactions impact severity of chronic pain and treatment outcome.

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**CONFLICT OF INTEREST**

The authors report no conflicts of interest in this work.

**AUTHOR CONTRIBUTIONS**

All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content;
agreed to submit to the current journal; gave final approval of the version to be published; and agree to be accountable for all aspects of the work.

ENDNOTE

1 An interdisciplinary treatment according to the International Association for the Study of Pain (IASP).

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