

Original Research Article

Data-driven clustering of chronic pain profiles using Swedish national registry data: Towards individualized decision support in interdisciplinary rehabilitation



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ABSTRACT

Background: Chronic pain affects 20–30% of adults and is a leading cause of disability and societal cost. Interdisciplinary, team-based treatment (IDT) is the most comprehensive approach, yet outcomes vary widely, and long-term benefits are, on average, modest. We aimed to develop clinically interpretable patient clusters from routine pre-treatment intake data and to validate them externally using independent national registry indicators, as a foundation for data-driven clinical decision support.

Methods: We analyzed a nationwide cohort of 90,505 patients entering specialist IDT in Sweden. A theory-informed unsupervised approach was used to cluster biopsychosocial intake features from the Swedish Quality Registry for Pain Rehabilitation using k-means clustering. Internal validation assessed stability and separation, while external validation tested concordance between questionnaire-derived cluster structures and pre-intake sick-leave trajectories and medication prescriptions derived from national registers using the Mantel statistic and logistic regression.

Results: Eight distinct clusters were identified, characterized by differing constellations of pain severity, psychological distress, functional status, and pain duration. Registry indicators tracked with cluster burden: higher-severity clusters showed greater sick leave and more medication prescriptions. Concordance between questionnaire-based and registry-based distance matrices was moderate to strong (Mantel $r = 0.65$; $p = 0.0016$) and cluster membership was significantly associated with the registry-based features. Three pre-intake sick-leave trajectories (high/stable, medium/stable, and low/increasing) were observed and differed across clusters.

Conclusions: Population-scale unsupervised clustering of routine patient-reported data, externally validated with independent national registries and supported by longitudinal sickness-absence patterns, yields clinically interpretable subgroups with strengthened construct validity. This provides a scalable foundation for patient stratification and the development of future clinical decision-support tools to better target and monitor IDT in real-world care.

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1. Introduction

Chronic pain represents a major global health concern [1,2], affecting an estimated 20–30% of adults worldwide [2,3]. It impairs functional ability, reduces quality of life (QoL), contributes to mental health challenges [4,5], and is a leading cause of disability [6]. Chronic pain also imposes substantial demands on healthcare systems and social welfare programs, accounting for up to 4% of national GDP in high-income countries [7].

Interdisciplinary treatment (IDT) is widely considered the gold standard for managing severe chronic pain [8]. It integrates physical, psychological, and behavioral therapies to improve function and support return-to-work goals [3,9]. In Sweden, IDT is delivered at specialized rehabilitation units affiliated with the Swedish Quality Registry for Pain Rehabilitation (SQRP).

Despite its comprehensive approach, the long-term effectiveness of IDT remains modest [10–12], with small to moderate average treatment effects and substantial interindividual variability [3,13]. Up to 30% of patients may experience deterioration following otherwise standardized programs [10].

Tailored treatment strategies may enhance the clinical impact of IDT [14], and Clinical Decision Support Systems (CDSS) have been increasingly proposed as tools to support personalized care by generating evidence-based clusters [15,16], and are now also being proposed as components of IDT as complex interventions. Previous studies have applied clustering approaches to chronic pain populations in Sweden [17] and internationally [18], using algorithms such as hierarchical clustering, k-means, latent class analysis, and hybrid methods [19–22], primarily to generate population-level knowledge rather than to guide decision-making for individual patients. These studies have identified three to four meaningful subgroups characterized by differences in pain severity, psychological distress, social functioning, and prognosis [19–21,23]. The existing literature has relied primarily on self-reported data, small sample sizes, focused on relatively limited cluster solutions, or lacked external validation against independent registry-based outcomes [17–25].

Unlike earlier chronic pain clustering studies, the present work is based on a nationwide Swedish registry-linked cohort and aims to derive patient profiles using variables routinely available at specialist intake. By externally validating these profiles against independent medication and sick-leave registries, the study extends prior subgrouping work toward clinically usable, data-driven stratification. In this sense, the contribution is not only descriptive phenotyping but also the development of an informatics framework for future decision-support applications in IDT.

2. Methodology

2.1. Data Description

SQRP collects standardized Patient-Reported Outcome Measures (PROMs) at baseline (intake), post-program, and at a 12-month follow-up; the data in this study covered the period from 2009 to 2022. The inclusion criteria were (1) referral to specialized pain rehabilitation clinics and (2) completion of the intake survey.

The PROMs include the Numeric Rating Scale (NRS), Hospital Anxiety and Depression Scale (HADS), EuroQol-5 Dimensions (EQ-5D), 36-Item Short Form Survey (SF-36), Work Ability Index (WAI), and Multidimensional Pain Inventory (MPI). For the remainder of the manuscript, these PROMs are referred to as features.

SQRP records were linked to national registries curated by the National Board of Health and Welfare (NBHW; Socialstyrelsen), the Swedish Prescribed Drug Register and the National Patient (Health Care) Register, and by the Swedish Social Insurance Agency (SSIA; Försäkringskassan) via Micro Data for Analysis of the Social Insurance Register (MiDAS). The National Patient Register contextualized

specialist-care utilization and diagnoses but was not used as a primary validation metric.

All linkages were performed under ethics approval (Swedish Ethical Review Authority, Dnr 2023-01532-01) with General Data Protection Regulation-compliant governance using pseudonymized data. All analyses were performed in R version 4.4.0.

2.2. Clustering based on The Swedish Quality Registry for Pain Rehabilitation

The dataset used for patient clustering included only features from the SQRP, as these are the only data available to the clinic at the time of the visit. The features selected from the SQRP can be seen in Table 1, where all features in the final dataset are described. In this dataset (the three registries combined), 90,505 patients were included.

The eight features included from the SQRP were selected based on common outcomes in pain research and represent core biopsychosocial domains routinely available at intake in specialist pain rehabilitation, while also maintaining sufficient completeness for robust clustering. Even though more than 25 features were initially considered (from instruments described under 2.1), the ones included in the dataset had less than 50% missing values as a screening rule when the actual missingness was around 5% for most features with only one exceeding 10% (Table 1).

For the features that were included in the dataset, imputation of missing values was performed through Multivariate Imputation by Chained Equations (MICE) [26] using predictive mean matching (*mice* library in R).

2.3. Selection of number of clusters

K-means clustering was used to cluster the patients into groups of similar pain patterns. All features were scaled before k-means was applied. The number of clusters was decided based on an elbow plot of the within cluster sum of squared errors (WCSS) and cluster stability measures. Additional measures (Silhouette score, Davies-Bouldin index, and Calinski-Harabasz index) were also evaluated during this process. The measures of cluster-wise stability were assessed through resampling and repeatedly generating the same number of clusters 100 times with bootstrap samples of the original data. Up to 20 clusters were evaluated. Cluster stability was calculated using the Jaccard coefficient of the similarity between clusters created through the bootstrap runs. The *clusterboot* function from the library *fpc* was used for this process.

Cluster differences in each variable were assessed using one-way ANOVA with cluster membership as the grouping factor. Effect sizes (η^2) were computed as the proportion of variance explained by clusters, and p-values were FDR-adjusted to control for multiple testing.

2.4. Longitudinal clustering of sick leave patterns

For every patient in the dataset, the sick-leave data were summarized for the 12 months before their first visit to the clinic. For this analysis 57,440 patients were used and sub-analyses were restricted to patients with the relevant linked registry data available. Since the data in the MiDAS register were provided in terms of spells of sick leave with the corresponding percentage, we converted the period provided into months and for each month we extracted the average percentage. Therefore, for each patient the 1-year period before the first visit to the clinic was transformed into a uniform length of 12 observations (months). With a time-series of 12 observations per patient we then performed longitudinal clustering to match patients of similar trajectories. As recommended by Den Teuling et al. (2023) [27], a two-step approach using growth curve modeling and k-means (GCKM) was applied for clustering these data (library *latrend* and *lme4* in R). This method is preferred because of its computational efficiency and has similar performance to the top algorithms used for longitudinal

Table 1

Demographic characteristics of the patients and feature description of the common dataset from the three registers (n = 90505). The features in **bold** are used for clustering and the features in *italic* for validation.

Feature name (range)	Short description of features and possible range	Category distribution or mean values (interquartile)	Percentage of missing values
Age	The age of the patient at first visit	44.9 (36–54)	0%
Sex	The sex of the patient	66,221F / 24284 M	0%
Pain duration (year)	How many years the patient has had pain	9.1 (1.96–13.17)	12.4%
MPI-SCI (0–6)	Multidimensional Pain Inventory self-reported questionnaire mean values	3.9 (3.41–4.55)	5.7%
NRS (0–10)	Numeric Rating Scale (Pain intensity over the last week)	6.9 (6–8)	4.4%
HADS anxiety (0–21)	Total anxiety experienced based on HADS questionnaire	9.5 (6–13)	6.1%
HADS depression (0–21)	Total depression experienced based on HADS questionnaire	9.0 (5–12)	5.5%
Rating Scale from EQ-5D	Actual health status as self-reported by patients (0–100), related to quality of life	40.4 (25–55)	7.4%
<i>Trajectory</i>	Which sick-leave trajectory the patient has based on prior 12 months (1–3)	12767 1/ 10158 2/ 34515 3	0%
<i>Neuro-pathic pain medication</i>	If medication for neuropathic pain has been prescribed in the last 6 months (0/1)	56,164 0/ 34,341 1	0%
<i>Opioids</i>	If opioids have been prescribed in the last 6 months (0/1)	55469 0/ 35036 1	0%
<i>Depression medication</i>	If antidepressant medication pain has been prescribed in the last 6 months (0/1)	61466 0/ 29039 1	0%
<i>Paracetamol</i>	If paracetamol has been prescribed in the last 6 months (0/1)	50717 0/ 39788 1	0%
<i>NSAID</i>	If nonsteroidal anti-inflammatory medication has been prescribed in the last 6 months (0/1)	56,110 0/ 34,395 1	0%
<i>Sleep medication</i>	If medication for sleep issues has been prescribed in the last 6 months (0/1)	68399 0/ 22106 1	0%

Abbreviations: MPI-SCI-Multidimensional Pain Inventory scale, NRS-Numeric Rating Scale, HADS-Hospital Anxiety and Depression Scale, EQ-5D-EuroQol-5 dimensions, NSAID-Nonsteroidal anti-inflammatory drugs.

clustering.

To decide on the number of trajectories used in this analysis, objective functions were evaluated, such as within cluster sum of squared errors (WCSS) and log-likelihood-based information criteria (AIC and BIC), but the final evaluation was on the quality of the trajectories created (how many were detected and the number of patients in each).

2.5. Evaluation of medication prescriptions of patients

The data available in the Swedish Prescribed Drug Register from the

National Patient Register were summarized in categories based on an expert panel discussion between M.H. (pharmacist and nurse), J.Ä. (medical doctor), and E.T. (physiotherapist). The 415 Anatomic Therapeutic Chemical (ATC) classification codes in the register (that described the medicine at the substance level) were summarized into six relevant categories of medication prescriptions for chronic pain management (according to different therapy areas, irrelevant areas were dismissed), specifically: medication to treat “Neuropathic pain”, “Opioids”, “Paracetamol”, Nonsteroidal anti-inflammatory medication “NSAID”, medication to assist with “Sleep”, and “Antidepressants”. The quoted names are the feature names created from this dataset.

For each patient, the medication prescription data was extracted for the six months before the first visit to the clinic. The choice of six months assumed, with domain knowledge, that medication prescription would be rather stable, without extensive fluctuations at this timepoint, close to the rehabilitation initiation. The six features created were binary, with a value of 0 if the patient had not been prescribed the specific medication category in the time frame of interest and 1 if they had.

2.6. Validation strategy

We evaluated whether the clusters created based on SQRP correspond to the objective data from the two registers (MiDAS and the Swedish Prescribed Drug Register), which were not used in the clustering process and thus provide independent data sources for external validation. For this work, two different sets of clusters were evaluated. Following the creation of the clusters based on the SQRP data, all data were summarized descriptively by cluster. Then, a different set of cluster centroids was calculated for the features that were not part of the clustering process (medication and sick-leave data), as seen in [Table 1](#). Two distance matrices were created, one for the first set of centroids and one for the second set of centroids. Following this, a Mantel test was run to test for the correlation between the two distance matrices. A significant correlation would indicate that the structures uncovered during the clustering process are preserved in the data that were not part of the clustering, thereby supporting the generalizability and external validity of the identified clusters.

Furthermore, we fitted logistic regression models for the external registry features. Sick-leave trajectories and medication types were used as responses (in multinomial and binary logistic regression, respectively) to further examine the consistency of cluster membership with independent clinical and utilization outcomes, with cluster membership, age, sex, and pain duration as predictors.

3. Results

In total, eight patient clusters were developed based on the highest number of clusters at which the Jaccard coefficient was over 0.8, the elbow point of the within-cluster sum of squares (WCSS), and the number of patients within each clusters ([Fig. 1](#)). For this solution, the Davies-Bouldin index was the lowest, whereas the Calinski-Harabasz index was consistent with the elbow criterion. The Silhouette plot favored lower numbers of clusters. The clusters reflected multidimensional separation of patients, with pain severity, mental health, quality of life, sex, and pain duration all contributing to the observed profiles. The clusters created corresponded well with the registries used for external validation, with moderate-to-high correlation between the distance matrices and a low p-value for the Mantel test.

3.1. Developing and validating the clusters

The eight patient clusters developed from the SQRP can be represented as radar charts in [Fig. 1](#) (light blue color). Radar charts facilitate visual comparison of multiple clusters and identifying patterns in data. The two other registers (MiDAS and the Swedish Prescribed Drug Register) were then used to validate the clusters and provide further insights

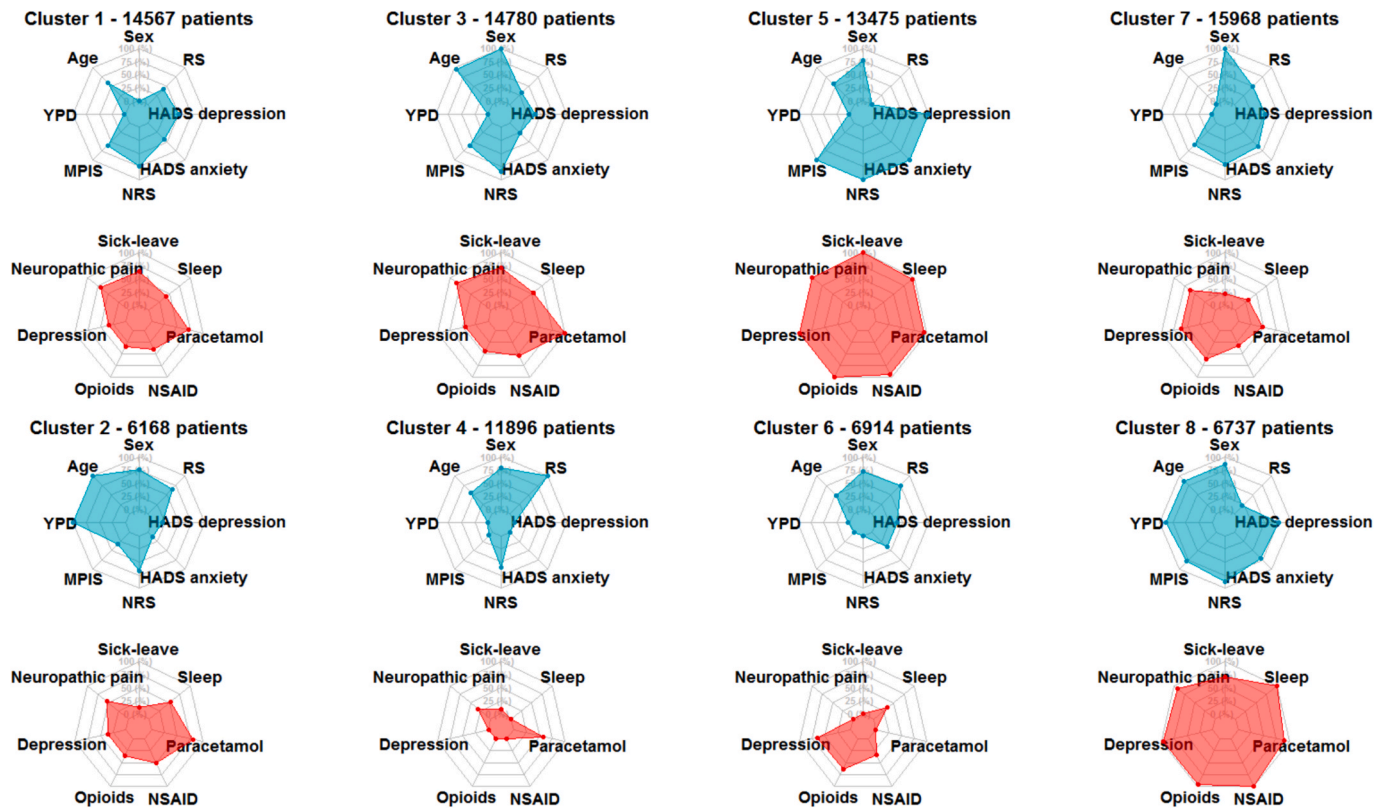


Fig. 1. The eight clusters that were developed based on the similarities of the SQRP features (In blue, Sex to RS, counter clock- wise), using WCSS. The radar charts in red show the sick leave trajectories and medication prescriptions for the same clusters. Values are normalized for min and max of the clusters. Abbreviations: YPD-Years of Pain Duration, MPIS-Multidimensional Pain Inventory scale, NRS-Numeric Rating Scale, HADS-Hospital Anxiety and Depression Scale, RS-Rating Scale, NSAID-Nonsteroidal anti-inflammatory drugs.

into the patients’ backgrounds. These are presented in red in Fig. 1. All cluster summaries are presented in Table 2.

The clusters show (in light blue) is that there was a clear separation of patients based on their responses to the SQRP questionnaire. There were clusters where the patients experienced high pain intensity and mental health challenges (Clusters 5 and 8), with the lowest QoL. Cluster 5 included patients with shorter pain duration and Cluster 8 included patients with longer pain duration. Patients in Clusters 1 and 7 had the same pain profile but differed in sex and age and weakly corresponded with Cluster 3. Patients in Clusters 4 and 6 had the highest QoL and dealt with average or low pain intensity. Finally, patients in Cluster 2 had many years of pain, were older, and had medium levels of pain and life satisfaction. A heatmap of the cluster mean profiles, related to each other, can be seen in Fig. 2, where the separation of the clusters matches what is shown in Fig. 1.

One-way ANOVAs showed significant between-cluster differences for all features (all FDR-adjusted $p < .001$). Effect-size estimates revealed that pain duration ($\eta^2 = 0.60$), MPI ($\eta^2 = 0.58$), and sex ($\eta^2 = 0.57$) were the strongest contributors to cluster discrimination, followed by depression ($\eta^2 = 0.52$), anxiety ($\eta^2 = 0.50$), and pain intensity ($\eta^2 = 0.47$). Rating scale and age showed moderate effects ($\eta^2 = 0.36$ and 0.28).

3.2. Trajectories of sick leave patterns and medication prescription

Using GCKM clustering, three sick-leave clusters emerged. These will be referred to as trajectories for the remainder of the paper. As shown in Fig. 3, the three trajectories are distinct: one with stable but medium sick leave (trajectory 2), one with increasing but low sick leave (trajectory 3), and one with high but decreasing sick leave (trajectory 1). When critically evaluating the number of clusters, AIC and BIC criteria favored

higher-dimension solutions, whereas cluster dispersion measures favored smaller numbers of clusters. The largest gain occurred when moving from two to three trajectories, whereas higher-order solutions primarily subdivided the same patterns by baseline level rather than temporal shape. Based on the principle of parsimony, balancing information gain against complexity, the three-trajectory solution was retained as the most interpretable summary of the sick-leave data. The percentage of patients in each trajectory can be seen in Table 1 and Table 2.

Similarly, the number of patients that had used the six medication categories can be seen in Table 2. Medication for neuropathic pain, opioids, and NSAID were used the most, whereas sleep medication was prescribed the least.

3.3. Validation of clusters based on sick leave trajectories and medication prescriptions

The sick-leave trajectories can be used to validate the clusters created. As seen in Fig. 1, Cluster 5 had the highest sick leave, followed by Clusters 8, 1, 3, and 7, as expected. Cluster 8 had patients with many years of pain compared to cluster 5 and had lower sick leave. Clusters 2, 4, and 6 had the lowest sick leave. In this context high sick leave means that the patients belonged to either trajectory 1 or trajectory 2, when low sick leave would correspond to trajectory 3.

When evaluating the medication prescriptions of the patients, we observed consistency between the challenges the patients experienced and the medication they received. Patients in Clusters 5 and 8 had the highest number of medication prescribed, while patients in Cluster 4 were mostly prescribed paracetamol. Patients in Clusters 1 and 3 had similar medication profiles, whereas patients in Cluster 7 (younger females) received more opioids and antidepressants. Patients in Cluster 2

Table 2
Cluster average values for the features used for clustering and validation.

Cluster	DTI		Sex (F)	Age	YWP	MPI	NRS	HADS- A	HADS- D	Rating scale	Cluster trajectories			NP	OP	DM	PM	NSAID	Sleep
	0	1									1	2	3						
1	59%	41%	0%	45.3	6.5	4.06	7	9.1	9.3	38.6	25%	18%	57%	39%	48%	27%	44%	38%	23%
2	56%	44%	76.9%	53.8	28.9	3.46	6.6	5.6	5.7	48.3	16%	18%	66%	36%	40%	27%	47%	37%	25%
3	53%	47%	99.9%	52.7	5.6	4.07	7.6	7.2	8	34.8	26%	19%	55%	42%	41%	30%	53%	41%	26%
4	58%	42%	79.3%	44.5	5.6	2.91	6.2	4.2	3.3	62.2	15%	18%	67%	30%	39%	16%	40%	39%	1.4%
5	61%	39%	77.8%	44.4	6.1	4.98	8.4	15.5	15	22	32%	17%	51%	46%	45%	46%	51%	41%	35%
6	50%	50%	73%	42.9	6.4	2.72	3	8.7	8	52.4	1.4%	16%	70%	23%	19%	35%	28%	26%	21%
7	50%	50%	100%	32.7	6	4.05	6.8	11.3	9.3	42.1	18%	16%	66%	37%	34%	34%	37%	37%	21%
8	57%	43%	85.5%	51	26.3	4.50	7.7	12.2	12.2	30.4	26%	18%	56%	44%	44%	45%	50%	39%	36%

Abbreviations: DTI- Interdisciplinary, team-based treatment, YWP-years with pain, MPI-Multidimensional Pain Inventory, NRS-Numeric Rating Scale, HADS-Hospital Anxiety and Depression Scale, EQ-5D-EuroQoL-5 dimensions, NP-Neuropathic pain, OP- Opioids, DM-Depression medication, PM-Pain medication, NSAID-Nonsteroidal anti-inflammatory drugs.

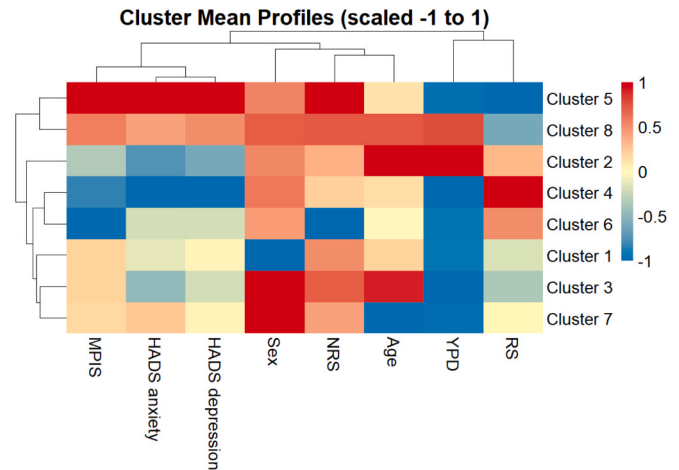


Fig. 2. Heatmap of the cluster mean profiles.

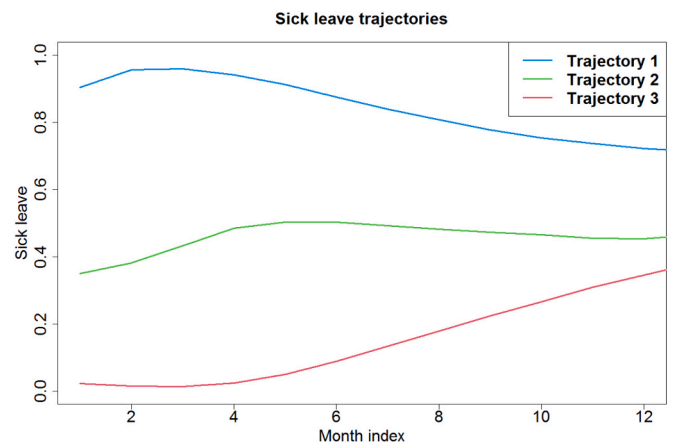


Fig. 3. The three sick leave trajectories for 57,440 patients in the dataset. Trajectory 1 with patients of consistently high sick leave, trajectory 2 with patients of medium but stable sick leave, and trajectory 3 with patients of low but increasing sick- leave. On the y-axis the percentage of sick leave is shown and, on the x-axis, the 12 months before the first visit to the clinic.

received a range of medications and patients in Cluster 6 were mostly prescribed antidepressants, opioids, and sleep medication.

More importantly, in addition to the visual confirmation of the agreement between the subjective and the objective data, the Pearson correlation between the distance matrices of the two sets of centroids (blue and red in Fig. 2) was 0.65, indicating moderate-to-high correlation between structures. The p-value of the Mantel test was 0.0016, suggesting that the cluster separation pattern in the first set is meaningfully preserved in the second set of centroids. In additional external validation analyses, cluster membership was strongly associated with registry-derived sick-leave trajectory in multinomial logistic regression, both in the unadjusted model and after adjustment for age, sex, and pain duration (likelihood-ratio tests, both $p < 0.001$). Likewise, cluster membership was significantly associated with all six medication categories in binary logistic regression models, both before and after adjustment (all $p < 0.001$).

3.4. Evaluation of whether the patients received treatment

The percentage of patients who received treatment in each cluster is shown in Table 2. The percentages in the clusters were between 39% and 50%, with the highest disagreement in cluster 5. Clusters 1, 2, 4, and 8 also had a high percentage of patients that did not receive treatment,

whereas clusters 6 and 7 were the only clusters where half the patients were selected for treatment.

4. Discussion

Based on the largest Swedish cohort to date of patients with chronic pain, we identified eight distinct patient clusters. The choice of registries for validation was strategic, as they contain information not typically captured by self-reported questionnaires, allowing for an objective and independent assessment of the derived clusters. This strengthens confidence that the eight-cluster solution reflects clinically meaningful phenotypes. The separation between clustering (SQRP) and validation (NBHW, SSIA) is a key methodological strength, ensuring that the clusters reflect information available in clinical practice while the validation anchors the findings in real-world outcomes. Because the clustering variables are routinely collected at intake, a future implementation could assign new patients to the nearest cluster profile at assessment and use that profile to support stratified triage, multidisciplinary focus, and outcome monitoring alongside clinician judgment.

The number of sick-leave trajectories was determined in a data-driven manner. We identified three distinct sick-leave trajectories: one with increasing sick leave and two relatively stable, either at a high or low level. When additional trajectories were specified, similar temporal patterns emerged with only minor differences in baseline levels, suggesting that the selected solution captured the essential structure of the data without introducing unnecessary interpretive complexity.

Radar charts were selected to visualize the cluster profiles, as they facilitate comparison across multiple dimensions and highlight distinct patterns between groups. Importantly, the external validation was not based solely on visual inspection (Fig. 1); rather, the correspondence between the two cluster sets was formally evaluated using a Mantel test and logistic regression.

Evaluation of the clusters in relation to subsequent receipt of IDT showed a largely balanced distribution of patients who did and did not receive IDT. This pattern is consistent with the premise that referral decisions are influenced by clinically salient determinants that are only partially captured [28], such as clinician assessment, contextual factors, and patient preferences. At the same time, baseline medication patterns were generally consistent with symptom profiles, suggesting that prescribing practices prior to rehabilitation broadly reflected clinical presentation and thereby provide an additional, clinically intuitive anchor for the cluster profiles.

Our eight-cluster solution builds on earlier work that applied hierarchical clustering, latent class analysis, or hybrid algorithms in chronic pain populations [18–24]. Whereas most previous studies reported three to four broad subgroups driven primarily by pain severity, psychological distress, and social functioning [19–21,23], the present analysis suggests that greater phenotypic granularity can be achieved when clustering is combined with large registry-linked cohorts and external validation. In particular, earlier Swedish work emphasized the importance of psychosocial and social-support dimensions [23], and large-scale studies highlighted severity-based groupings with prognostic implications [20]. These findings are consistent with the multidimensional profiles observed here but further differentiated in our eight-cluster solution. The present results therefore complement mechanism-based approaches such as ROPA [22] by demonstrating that registry-validated clustering can support more refined stratification within biopsychosocial pain models.

Taken together, these findings extend previous clustering studies in chronic pain populations [17–23] by demonstrating that a more detailed eight-cluster solution can be externally validated using objective registry data. This approach supports a more nuanced characterization of patient heterogeneity and may contribute to the development of more precisely targeted rehabilitation strategies.

5. Conclusions and Future Work

Socioeconomic and demographic data from Statistics Sweden, as well as additional healthcare utilization data, will be incorporated in future analyses to further enrich patient profiles and support even more comprehensive cluster validation. Moreover, the findings regarding sick-leave trajectories need to be investigated in a more thorough, using additional data processing techniques. The results from the Mantel test should be interpreted with caution, but both the test results and the visual inspection suggest similar cluster structures across the registries.

As part of future work, we will examine which patients in each cluster received treatment and compare their outcomes with those of patients who did not. Since data are available for at least five years following the initial assessment, sick-leave patterns and changes in medication prescription can be followed.

This work is an initial step toward individualized decision support for modeling patient trajectories [29], and several limitations should be considered. First, the cohort represents patients referred to specialized pain rehabilitation in Sweden and may not be representative of all chronic pain populations or other healthcare systems. Second, although the final clustering variables had relatively low missingness overall, imputation was required for some intake variables and may have introduced uncertainty. Third, as in all unsupervised analyses, the retained cluster and trajectory solutions should be viewed as useful and clinically interpretable representations of the data rather than uniquely true latent structures. Finally, the proposed relevance for clinical decision support remains foundational and requires prospective evaluation, workflow integration, and transportability testing before implementation.

CRedit authorship contribution statement

Ilias Thomas: Writing – review & editing, Writing – original draft, Visualization, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Roger Nyberg:** Writing – review & editing, Writing – original draft. **Riccardo LoMartire:** Writing – review & editing, Data curation. **Tony Bohman:** Writing – review & editing, Project administration, Funding acquisition. **Elena Tseli:** Writing – review & editing, Methodology. **Johan Arnlov:** Writing – review & editing, Methodology. **Anna Grimby-Ekman:** Writing – review & editing. **Linda Vixner:** Writing – review & editing, Funding acquisition. **Marika Hagelberg:** Writing – review & editing, Methodology. **Björn Ång:** Writing – review & editing, Methodology, Conceptualization Funding.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Johan Arnlov reports a relationship with AstraZeneca AB that includes: consulting or advisory and speaking and lecture fees. Johan Arnlov reports a relationship with Boehringer Ingelheim AB that includes: consulting or advisory and speaking and lecture fees. Johan Arnlov reports a relationship with Astellas Pharma AB that includes: consulting or advisory. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Declaration of generative AI and AI-assisted technologies in the manuscript preparation process

During the preparation of this work the authors used ChatGPT in order to review the code following revision. After using this tool/service, the authors reviewed and edited the content as needed and take full responsibility for the content of the published article.

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