TITLE PAGE

Title: Three subgroups of pain profiles identified in 227 women with arthritis: a latent class analysis

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ABSTRACT

Introduction: The objectives were to identify subgroups of women with arthritis based upon the multi-dimensional nature of their pain experience and to compare health and socio-demographic variables between subgroups.

Method: A latent class analysis of 227 women with self-reported arthritis was used to identify clusters of women based upon the sensory, affective and cognitive dimensions of the pain experience. Multivariate multinomial logistic regression analysis was used to determine the relationship between cluster membership and health and socio-demographic characteristics.

Results: A three-class cluster model was most parsimonious. 39.5% of women had a uni-dimensional pain profile; 38.6% of women had moderate multi-dimensional pain profile that included additional pain symptomatology such as sensory qualities and pain catastrophizing; and 21.9% of women had severe multi-dimensional pain profile that included prominent pain symptomatology such as sensory and affective qualities of pain, pain catastrophizing, and neuropathic pain. Women with a severe multi-dimensional pain profile have a 30.5% higher risk of poorer quality of life and a 7.3% higher risk of suffering depression, and women with a moderate multi-dimensional pain profile have a 6.4% higher risk of poorer quality of life when compared to women with uni-dimensional pain.

Conclusion: This study identified three distinct subgroups of pain profiles in older women with arthritis. Women had very different experiences of pain, and cluster membership impacted significantly on health related quality of life. These preliminary findings provide a stronger understanding of profiles of pain and may contribute to the development of tailored treatment options in arthritis.

Keywords: pain, osteoarthritis, rheumatoid arthritis, epidemiology, latent class analysis

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INTRODUCTION

Pain is a challenging clinical entity in the management of arthritis. Painful arthritis results in physical disability [1], decreased independence [1] and increased healthcare utilization [2]. Epidemiological studies attempting to asses the multi-dimensional experience of pain in arthritis are lacking, predominantly reporting only the intensity or severity of pain [3]. An Osteoarthritis Research Society International working group has directed a research agenda towards defining the disease state of osteoarthritis, with outcomes to improve the understanding of phenotypes of osteoarthritis that include the patterns and presentation of pain [4].

In 1965, Melzack and Casey proposed the gate control theory of pain [5]. This model emphasized the dynamic role of the brain in processing pain, and was the first to include psychological factors as an integral component. Melzack and Casey proposed three dimensions of the subjective pain experience: sensory-discriminative, affective-motivational and cognitive-evaluative [6]. Sensory-discriminative dimensions of the pain experience include intensity, location, quality and temporal aspects [6] The affective-motivational dimension reflects the emotional aspects of pain including feelings of unpleasantness and distress [7]. The cognitive-evaluative dimension comprises thoughts associated with pain, analyzing the cause of pain and determining appropriate behaviors in response to pain [8].

This model for the experience of pain is widely accepted, and whilst first described in the 1960's, is still relevant to the experience of pain today. More recently, Melzack and Katz postulated the neuromatrix theory of pain [6]. This theory explains pain as a dynamic process involving continuous interactions between complex ascending and descending neural circuitry [6]. It moves away from pain as a singular sensation, to an understanding of pain as a multidimensional experience generated by multiple influences.

Few studies have investigated subgroups of people with arthritis who differ in regards to their experience of pain. A study involving 129 older, community dwelling adults with self-reported knee or hip osteoarthritis, identified three subgroups based on pain and symptoms [9]. The authors concluded that people with osteoarthritis had symptoms other than joint pain, and that some symptoms may arise from the central nervous system as well as peripheral joint pathology [9]. In knee osteoarthritis, five profiles based on radiographic severity, lower extremity muscle strength, body mass index and depression were identified in 842 patients [10]. Most recently, Cruz-Almeida et al. [11], derived four psychological profiles in 194 persons with knee osteoarthritis and reported that each psychological profile displayed unique sets of clinical and somatosensory characteristics. In order to improve the understanding of the experience of pain in arthritis, subgrouping people with arthritis based upon the sensory, affective and cognitive dimensions of the pain experience would be of value. Therefore, the aim of this study was to identify subgroups of older women with arthritis based upon the multi-dimensional nature of their pain experience and to compare health and demographic variables between subgroups.

MATERIALS AND METHODS

Study design, participants, and setting

The Australian Longitudinal Study on Womens Health (ALSWH) is a longitudinal population-based survey that has been studying the health of a national sample of Australian women since 1996. Detailed methods for the recruitment and maintenance of the ALSWH cohorts have been described. In 2012, a cross-sectional sub study survey was sent to a sample of 700 community dwelling women from the ALSWH cohort born between 1946-1951. A postal survey was sent to 350 randomly selected women who answered 'yes' to the question "In the past three years, have you been diagnosed or treated for arthritis/rheumatism" in Survey 3 (2001) or Survey 4 (2004), and 350 randomly selected women who have never reported any form of arthritis in Surveys 3 – 6 (2001 – 2010). Women who wished to participate provided written consent and returned surveys. For all consenting women, health and demographic data from ALSWH Survey 6 (2010) was accessed and linked to the sub study survey data.

In the sub study, women who answered 'yes' to the question "In the past three years, have you been

diagnosed or treated for: osteoarthritis, rheumatoid arthritis, psoriatic arthritis, gout or other form of arthritis", were included in this analysis. Women with arthritis were asked: "Which of your joints have been troublesome (painful, aching, swollen or stiff) on most days of the past month?" and asked to complete a body homunculus. Women were asked to recall pain in light of their joint pain. For example, "rate the severity of joint pain", "the course of their joint pain" or "how intense each pain quality was in regards to the pain in your joints".

Details of the protocol for this sub study have been published [12]. This study was approved by the Human Research Ethics Committee of the University of Newcastle; Approval number: H-2012-0144.

Dimension of pain variables

The three dimensions of pain as defined by Melzack and Casey were used as an organizing construct. Six variables, consisting of a) the scores from three measures and b) three subscale scores from one measure, were used to assess the multidimensional nature of pain. The six variables are described below and were used as indicator variables in the latent class analysis (LCA) model.

The sensory-discriminative dimension of the pain experience was measured by the Graded Chronic Pain Scale (GCPS) [13], scores of two subscales of the McGill Pain Questionnaire (Short Form) (SF-MPQ) [14] and the painDETECT measure [15]. The GCPS consists of an underlying severity continuum defined by pain intensity and interference with daily activities [16]. The GCPS is graded into five ordinal categories [16] and the SF-MPQ present pain intensity (PPI) subscale six ordinal categories [14] (see Table 1). The score was dichotomized into the presence or absence of sensory qualities (cut-point, >10). Rationale for the SF-MPQ sensory subscale cut-point is below. The painDETECT measure is a self-report screening tool for neuropathic pain that consists of nine items that relate to sensory descriptors and the temporal and spatial characteristics of pain [15]. Scores ≤12 indicate a neuropathic pain component is unlikely, and scores ≥19 indicate likely neuropathic pain; scores between 13 -18 reflect a possible neuropathic pain component [15]. Similar to that of previous studies [17], this study used the lower cut-point of ≤12 to indicate the presence or absence of neuropathic pain.

The affective-motivational dimension of the pain experience was measured by the affective subscale of the SF-MPQ [14]. The score was dichotomized into the presence or absence of affective qualities (cut-point, >1). Rationale for the SF-MPQ affective subscale cut-point is below.

The cognitive-evaluative dimension of the pain experience was measured by the Pain Catastrophizing Scale (PCS). This a measure of the different perspectives on catastrophic thinking related to pain [18].

The score was dichotomized into the presence or absence of pain catastrophizing (cut-point, >5). Rationale for the SF-MPQ affective subscale cut-point is below.

It is common in clinical research to categorize people as having or not having a particular attribute, often to aid in the interpretation and presentation of data and translation of results [19]. Where no criterion-based cut-points are available, median scores can be used. There are, however, drawbacks to this method, such as reducing statistical power and underestimating variability [19]. Given that criterion-based cut points do not exist for the SF-MPQ, an a-priori decision was made to use median split for both sensory and affective subscales (>10, >1 respectively). The PCS scoring manual provides a 75th percentile distribution as a selected threshold for problematic pain catastrophizing [20], therefore the 75th percentile split for the PCS cut-point was >5.

Socio-demographic covariates

Covariates used to examine factors associated with the different pain profiles included health related quality of life (Medical Outcomes Study: 36 Item Short Form Survey (SF-36) [21], physical component scale (PCS) and mental component scales (MCS)); depression (CESD-10); area of residence ('urban' and 'rural') ; marital status; employment status; and Body Mass Index (BMI) ('underweight/normal', 'overweight' and 'obese' .

Statistical analyses

LCA was used to identify clusters of women with similar pain profiles. This method was chosen over other methods of latent variable analysis due to the ability to deal with missing data, include different data types and the elegant handling of outliers [22]. A LCA model was established to identify the minimal number of clinically meaningful clusters so that within-cluster variation is minimized whilst between-cluster variation is maximised. The LCA model then calculated the likelihood of each participant belonging to their assigned cluster. The ideal number of clusters was identified based upon both goodness of fit indices and pragmatic evaluation. As there is no single statistic to determine goodness of fit, Bayesian Information Criterion (BIC) [23], Akaike's Information Criterion (AIC) and consistent AIC (cAIC) [24] were considered. In addition, the log likelihood (LL) and conditional bootstrap likelihood ratio tests (BLRT) were used to determine if successively adding another cluster improved model fit, up to a 10-cluster model [25]. Pragmatic evaluation considered the minimum average posterior probability (PP) of belonging to each cluster (>0.7), distinctiveness of cluster membership and the minimum practical cluster size.

Multivariate multinomial logistic regression (MLR) analysis was used to determine the relationship between cluster membership and health and socio-demographic characteristics [26]. The modified

Bolck-Croon-Hagenaars (BCH) approach was used for proportional classification of all participants [26]. The risk of belonging to each cluster for a given characteristic was compared to the reference cluster (defined by the cluster with the largest population) and expressed as a relative risk ratio (RRR). Testing for collinearity was performed with tolerance of <0.1, and variance inflation factor ≤0.2 or ≥5.0 indicating possible collinearity [27]. Full and reduced model predictive efficiency were examined using goodness of fit indices, mainly AIC [28], with the lowest score (AIC_{min}) indicating the better fitting model. Reduced models excluded combinations of the 3 least significant variables found on univariate analysis ($2^{\wedge 3}$- 1 = 7 reduced models tested).

A sensitivity analysis was conducted to compare cluster membership and response probabilities of pain variables for women who answered 'yes' to the question "In the past three years, have you been diagnosed or treated for: osteoarthritis", and then compared to the cohort of 227 women with arthritis.

STATA v13.1 (Stata Corp., College Station, TX, USA) was used to generate descriptive statistics of the sample, analyze model collinearity and predictive efficiency. Latent GOLD v5.0 (Statistical Corporation, Belmont, MA, USA) was used for LCA analysis and to generate the MLR model.

RESULTS

Sample

From 700 women invited to participate in the sub study, 579 consented to participate and returned surveys (82.7% response rate). All 227 women (39.2%) who self-reported arthritis were included in LCA. Nearly all women (97.4%) reported a doctor diagnosed their arthritis. Most women (98.2%) reported suffering painful, aching, stiff or swollen joints (symptomatic arthritis) at the time of the sub study. Health and socio-demographic characteristics of the total sample are presented in Table 2.

Latent class analysis

LCA goodness of fit indices and PP are presented in Table 3. The rate of change in LL diminished rapidly after the three-cluster solution; BIC_{LL} (min) and $cAIC_{LL}$ (min) favoured the three-cluster solution; AIC_{LL} (min) and the bootstrap likelihood ratio test indicated that up to a six-cluster solution was possible. The minimum average posterior probability for the three to six-cluster models was 87%, 88%, 82% and 77% respectively, all greater than the suggested minimum range [29]. Adding each cluster beyond the three-cluster model provided no additional clinically distinctive subgroups. Therefore, the three-cluster solution best satisfied model efficiency, parsimony, and ability to identify distinct subgroups of women. Health and socio-demographic characteristics of each cluster are presented in Table 2.

Characterization of clusters

Table 4 reports the overall proportions of each pain dimension variable count per cluster. Figure 1 visually depicts the proportion of response of each pain dimension variable per cluster. GCPS and SF-MPQ PPI proportion are shown per ordinal rank. Neuropathic pain, pain catastrophizing, sensory qualities and affective qualities are shown as proportion above the cut-point (≤12, >5, >10 and >1 respectively).

Cluster one comprised 39.5% of the sample (n = 95). In cluster one, 100% of women had GCPS Grade 1 and 58% had SF-MPQ PPI mild pain. As shown in Figure 1, 9% of women had neuropathic pain, 13% of women had pain catastrophizing and only 3% and 8% of women had sensory and affective qualities to their pain, respectively. Women in cluster one can be summarized as having pain that is mild in nature with no further symptomatology and are labeled as having a uni-dimensional pain profile.

Cluster two comprised of 38.6% of the sample (n = 83). In cluster two, 64% of women had GCPS Grade 2 and 86% of women had SF-MPQ PPI discomforting pain. As shown in Figure 1, 14% of women had neuropathic pain, 40% of women had pain catastrophizing, 49% of women had sensory qualities to their pain and 30% of women had affective qualities to their pain. Women in cluster two can be summarized as having pain of a moderate severity with additional pain symptomatology and are labeled as having a moderate multi-dimensional pain profile.

Cluster three comprised 21.9% of the sample (n = 49). In cluster three, 53% of women had GCPS Grade 4. As shown in Figure 1, 37% of women had SF-MPQ PPI discomforting pain, 28% had SF-MPQ PPI distressing pain, 24% had SF-MPQ PPI horrible pain and 11% of women had SF-MPQ PPI excruciating pain. A total of 65% of women had neuropathic pain and 82% of women had pain catastrophizing. A very considerable 98% and 95% of women had sensory qualities and affective qualities to their pain, respectively. Women in cluster three can be summarized as having pain of a severe nature with prominent pain symptomatology and are labeled as having a severe multi-dimensional pain profile.

Multinomial logistic regression

MLR compares socio-demographic characteristics between clusters, with cluster one (uni-dimensional pain profile) as the reference cluster. There was low chance of collinearity (tolerance range = 0.57 to 0.96; mean VIF = 1.29) when all variables were included. The AIC statistic, used to evaluate the seven reduced models for best fit, achieved minimum value after removal of the variable employment (AIC_{min} = 375.4), when compared to the full model (AIC = 378.5). The reduced model used in MLR included residence, marital status, BMI, quality of life (SF-36 PCS, MCS) and depression. Figure 2 shows the RRR of belonging to cluster two or cluster three, compared to cluster one. RRR for

continuous variables are expressed per standard deviation (SD) decrease for SF-36 PCS and MCS, and per SD increase for CESD-10 depression.

Comparisons of health and socio-demographic factors between clusters

Women in cluster two who lived rurally were less likely to experience moderate pain intensity and moderate pain symptomatology compared to women in cluster one (RRR = 2.7, 95% CI: 1.1 to 6.7). Conversely, women in cluster two who had lower quality of life (SF-36 PCS) were more likely to experience moderate pain intensity and moderate pain symptomatology compared to women in cluster one (RRR = 6.4, 95% CI: 2.6 to 17.4) Women in cluster three who had lower quality of life (SF-36 PCS) and higher depression (CESD-10), were more likely to experience severe pain intensity and prominent pain symptomatology compared to women in cluster one (RRR = 30.5, 95%CI: 11.4 to 88.9; RRR = 7.3, 95%CI: 1.2 to 53.9 respectively).

Sensitivity analysis

Of the 227 women in the arthritis cohort, 73.1% of women (n = 166) self-reported osteoarthritis. When the osteoarthritis only group was analysed using latent class analysis, 12.6% of women (n = 21) were re-classified as belonging to the next highest cluster (cluster one as cluster two (6.0%, n=10), cluster two as cluster three (6.6%, n=11)), when compared to women with arthritis group. Overall, the cluster distribution remained similar between the two groups, with relative membership change of -0.3%, 1.4%, -1.1% for clusters one to three respectively.

The majority of pain characteristics that described each cluster altered in distribution by less than 5%. Distribution change of greater than 5% was observed in clusters two (7% increase in GCPS score =1; 8% decrease in proportion of neuropathic pain; and 8% decrease in proportion of SF-MPQ sensory quality), and in cluster 3 (12.5% decrease in proportion of SF-MPQ affective quality), when compared to the arthritis group. All differences in proportion of pain characteristics for cluster one were less than 5% for women with osteoarthritis when compared to the arthritis group.

DISCUSSION

This study identified three subgroups of community dwelling, older women based on their experience of pain in arthritis. The distinct pain profiles of each subgroup were characterized by women with a uni-dimensional pain profile, that is they have mild pain and no further symptomatology (cluster one; 39.5% of the sample); women with a moderate multi-dimensional pain profile that includes moderate pain and some pain symptomatology (cluster two; 38.6% of the sample); and women with a severe multi-dimensional pain profile who have horrible pain and prominent pain symptomatology (cluster three; 21.9% of the sample). Of interest, nearly 60% of women with arthritis have a multi-dimensional experience of pain. In a subgroup of one fifth of the women, all women have sensory qualities such as

throbbing, shooting and stabbing pain, as well as affective qualities such as tiring, sickening and punishing pain. In this severe multi-dimensional pain profile subgroup 80% of women have catastrophic thinking related to their pain and 65% of women have neuropathic pain. Our findings assist as a preliminary study of the experience of pain in arthritis, and by including multiple dimensions of pain in a robust statistical latent class analysis, show that women with arthritis have very different experiences of pain.

The mean duration of arthritis was 11 years, which is consistent with mean duration in osteoarthritis [9], knee osteoarthritis [30] and rheumatoid arthritis [31]. The time since onset of current painful episode was typically 1-3 months, supporting the understanding that arthritis is a chronic condition with pain fluctuation [32]. Understanding of the experience of pain in arthritis includes the complex interaction between nociceptive and neuropathic mechanisms [33, 34]. Evidence advocates the relationship between central sensitisation and neuropathic pain mechanisms and the traditionally peripheral disease of arthritis [35] and focus groups have described pain in arthritis that is suggestive of neuropathic pain [36, 37]. Of the women subgrouped as having a moderate multi-dimensional pain profile, 14% experienced neuropathic pain and in the severe multi-dimensional pain profile subgroup, 65% of women experienced neuropathic pain. Of the women subgrouped as having a moderate multi-dimensional pain profile, half of the women had sensory qualities of pain and one third had affective qualities of pain. In the severe multi-dimensional pain profile subgroup, nearly all women had sensory and affective qualities to their pain (98% and 95% of women respectively). As visualized in Figure 1, there is a clear and distinct increase in the proportion of response of each pain dimension in each subgroup. Therefore, it is also shown that with higher proportions of severe pain intensity comes a higher proportion of pain symptomatology. Previous studies concluded that, as subgroups of people with arthritis have differing symptomatology, groups with more severe symptoms have symptoms as a result of the manifestation of central nervous system contributions [11, 31, 9]. Results from this study highlight not only a neuropathic pain component to arthritis pain, but reflect different degrees of the pain experience, and possibly an overlap between nociceptive and neuropathic pain mechanisms. Our findings lend support to the hypothesis that nociceptive and neuropathic pain are related entities that exist at different points on the same continuum [38].

Membership in either cluster two or three had a significant impact on quality of life compared to membership in cluster one. Particularly, women with a severe multi-dimensional pain profile have on average a 30.5% higher risk of poorer quality of life and a 7.3% higher risk of suffering depression when compared to women with uni-dimensional pain. Women with a moderate multi-dimensional pain profile have on average a 6.4% higher risk of poorer quality of life when compared to women with uni-dimensional pain. This study is the first to identify subgroups of women with arthritis based on their different experiences of pain. Whilst there are both arguments for and against subgrouping

[39], subgrouping for targeted treatment models in low back pain have been shown to maximise treatment benefit, reduce harm, decrease costs and increase healthcare efficiency [40, 41]. Stratified care for low back pain involves targeting treatment to subgroups of patients based on characteristics such as prognostic factors, response to treatment and underlying mechanisms [42]. A targeted treatment approach is gaining interest due to prognostic diversity and differences in treatment response in various conditions that have high diagnostic and therapeutic uncertainty [43]. Stratification of arthritis patients based on underlying mechanisms may be important as neuropathic pain is poorly controlled by common analgesics [44] and people with neuropathic pain are more likely to respond to targeted analgesia (including gabapentinoids) than to non-steroidal anti-inflammatory drugs [38]. In light of the findings of this study, treatment stratified on the type of pain in arthritis would be of value as improved outcomes may include a shift in cluster membership, decreasing the risk of poor quality of life and depression. Additionally, cognitive factors are just as important as physiological factors, and cognitive behavioural intervention approaches have been shown to be effective in managing pain in arthritis [45]. Whilst in its infancy, the stratified subgrouping of people with arthritis is warranted to inform tailored treatment interventions (both pharmacological and non-pharmacological), potentially improving clinical outcomes and management of the experience of pain in arthritis.

Subgrouping of people with rheumatoid arthritis and osteoarthritis have found clusters that represented high, intermediate and low levels of pain, fatigue and various symptomatology [31, 9]. When LCA was applied to the osteoarthritis group (73.1%; n = 166), a small proportion of women were reclassified into the next highest cluster. However, cluster membership size remained proportionally. For women with osteoarthritis, the distribution of pain profile severity marginally favored the milder clusters. The difference in distribution of pain symptomatology was small when the osteoarthritis group was compared to the arthritis group. Therefore, it was appropriate to pool as arthritis for subsequent regression analysis, which allowed for exploration of variables without over fitting. These findings suggest that the majority of women with osteoarthritis reported moderate or severe multi-dimensional pain profiles, and is the first to demonstrate that women reported multidimensional pain with a range of severities regardless of arthritis type.

Strengths and Limitations

The strength of this study lies within the robust statistical methodology applied to the identification of subgroups of women. The average PP of cluster membership was 0.87 or higher, suggesting most participants were correctly classified. The use of a three-step methodology resulted in wider confidence intervals than other, less robust, approaches to analysis. The sample size (n=227) is larger than any recent subgrouping studies in arthritis (n=129, n=169 and n=194 [9, 11, 31]).

Limitations include the dichotomization of pain variables may be seen as inappropriate, it is difficult to describe meaningful clusters if variables are analyzed as continuous data. Whilst preserving continuous data allows accuracy, it may make interpretation complicated. Dichotomizing variables creates an assumption that allows improved interpretability, generating meaningful and relevant findings for the clinician. While cut-points may be subjective in nature, cut-points were determined a-priori. The use of self-report diagnosis on arthritis is also a limitation. Incorporating a clinical assessment or radiological findings of arthritis, and essentially utilizing classification criteria, would be beneficial for future clinical studies.

CONCLUSION

This study identified three subgroups of older, community dwelling women with arthritis with very different, very distinct profiles of pain. Two fifths of women had a moderate multi-dimensional pain and one fifth had severe multi-dimensional pain. Women with moderate and severe multi-dimensional pain profiles were at a significantly greater risk of poorer physical and mental health related quality of life. For clinicians, it is important to be aware that subgroups of women with arthritis exist, and have very different experiences of pain.

ABBREVIATIONS

AIC: Akaike's Information Criterion; AIC_{min}: Akaike's Information Criterion lowest score; ALSWH: Australian Longitudinal Study on Womens Health; BCH: Bolck-Croon-Hagenaars; BLRT: bootstrap likelihood ratio tests; BMI: body mass index; CI: confidence interval; cAIC: consistent Akaike's Information Criterion; CESD-10: Center for Epidemiologic Studies Short Depression Scale; GCPS: Graded Chronic Pain Scale; LCA: latent class analysis; LL: log likelihood; MLR: multivariate multinomial logistic regression; PCS: Pain Catastrophizing Scale; PP: posterior probability; RRR: relative risk ratio; SF-MPQ: McGill Pain Questionnaire (Short Form); SF-MPQ PPI: McGill Pain Questionnaire (Short Form) present pain intensity subscale; SF-36: Medical Outcomes Study: 36 Item Short Form Survey; SF-36 MCS: Medical Outcomes Study: 36 Item Short Form Survey mental component scale; SF-36 PCS: Medical Outcomes Study: 36 Item Short Form Survey physical component scale; SD: standard deviation.

AUTHOR'S CONTRIBUTIONS

KD, LP, FB and JB made substantial contributions to the design and the acquisition of data. KD and AD conducting the statistical analysis. All authors made substantial contributions to the interpretation of data, have been involved in drafting the manuscript and have given final approval of the version to be published.

CONFLICT OF INTEREST

The authors declare they have no conflicts of interest.

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TABLES

Table 1: Ordinal categories of the Graded Chronic Pain Scale and the McGill Pain Questionnaire (Short Form) present pain intensity subscale

Graded Chronic Pain Scale	
Grade 0	Pain Free
Grade 1	Low intensity, low interference
Grade 2	High intensity, low interference
Grade 3	Moderate interference with activities
Grade 4	Severe interference with activities
McGill Pain Questionnaire (Short Form) present pain intensity subscale	
0	No pain
1	Mild pain
2	Discomforting pain
3	Distressing pain
4	Horrible pain
5	Excruciating pain

Table 2: Socio-demographic characteristics of the total sample and socio-demographic characteristics by cluster.

Characteristic	Total	By cluster		
		Cluster 1 ***Uni-dimensional pain profile***	**Cluster 2** ***Moderate multi-dimensional pain profile***	**Cluster 3** ***Severe Multi-dimensional pain profile***
	(n=227)	**(n= 95)**	**(n=83)**	**(n=49)**
Age (yrs), mean (SD)	64.6 (1.4)	64.5 (1.4)	64.7 (1.3)	64.6 (1.6)
Rural residence, n (%)	149 (65.6)	64 (43.0)	51 (34.2)	34 (22.8)
Married/de facto, n (%)	177 (78.0)	81 (45.8)	61 (34.5)	35 (19.8)
Employed, n (%)	104 (45.8)	35 (33.7)	38 (36.5)	31 (29.8)
WHO Body Mass Index classification, n (%)				
Normal / Underweight	64 (28.2)	31 (48.4)	24 (37.5)	9 (14.1)
Overweight	81 (35.7)	36 (44.4)	25 (31.0)	20 (25.0)
Obese	82 (36.1)	28 (34.2)	34 (41.5)	20 (24.4)
Depression, mean (SD)	6.5 (5.7)	4.6 (4.3)	6.0 (4.3)	11.1 (7.1)
SF-36 Physical component scale, mean (SD)	60.7 (10.9)	53.6 (7.6)	62.0 (8.3)	72.4 (9.2)
SF-36 Mental component scale, mean (SD)	49.4 (11.0)	47.2±10.4	48.8 (10.0)	54.8 (12.2)

Abbreviations

WHO: World Health Organisation; SF-36: Medical Outcomes Study: 36 Item Short Form Survey.

Table 3: Latent class analysis goodness of fit indices and posterior probabilities across one to ten cluster models.

Model	LL	L^2	AIC (LL)	cAIC(LL)	BIC (LL)	BLRT (L^2) p-value	Cluster (n): PP
1	-1029.05	749.82	2082.10	2135.20	2123.20	-	
2	-883.25	458.22	1804.50	1888.58	1869.58	<**0.001**	1 (n=136): 0.95
							2 (n=91): 0.95
3	**-853.98**	**399.67**	1759.96	**1875.01**	**1849.01**	<**0.001**	**1 (n=95): 0.91**
							2 (n=83): 0.88
							3 (n=49): 0.87
4	-841.15	374.01	1748.29	1894.32	1861.32	<**0.001**	1 (n=83): 0.88
							2 (n=78): 0.90
							3 (n=57): 0.88
							4 (n=9): 0.91
5	-830.03	351.78	1740.06	1917.06	1877.05	0.002	1 (n=79): 0.84
							2 (n=60): 0.82
							3 (n=63): 0.86
							4 (n=16): 0.90
							5 (n=9): 0.92
6	-822.08	335.88	**1738.17**	1946.14	1899.14	0.004	1 (n=68): 0.88
							2 (n=68): 0.88
							3 (n=56): 0.77
							4 (n=17): 0.91
							5 (n=10): 0.89
							6 (n=8): 0.86
7	-816.81	325.34	1741.62	1980.57	1926.57	0.082	
8	-811.60	314.92	1745.20	2015.12	1954.12	0.172	
9	-808.16	308.03	1752.32	2053.21	1985.21	0.418	
10	-805.20	302.11	1760.40	2092.27	2017.27	0.612	

Model indicates the number of clusters per model. The lowest value of BIC indicates the best fitting model. Posterior probability values close to 1 indicate good classification. Values shown in **bold** represent the best fitting model for that indicie.

Abbreviations

LL: log-likelihood; L^2: likelihood-ratio chi-squared statistic; AIC: Akaike's Information Criterion; cAIC: consistent Akaike's Information Criterion; BIC: Bayesian information criterion; BLRT: bootstrap likelihood ratio tests; PP: Posterior probabilities

Table 4. The overall proportions of each pain dimension variable count per cluster.

Pain dimension variables	Cluster 1 *Uni-dimensional pain profile* (n= 95)	Cluster 2 *Moderate multi-dimensional pain profile* (n=83)	Cluster 3 *Severe Multi-dimensional pain profile* (n=49)
Graded Chronic Pain Scale			
Grade 1	0.91	0.09	0.00
Grade 2	0.00	0.79	0.21
Grade 3	0.00	0.63	0.38
Grade 4	0.00	0.19	0.81
SF-MPQ PPI			
No pain	0.78	0.22	0.00
Mild pain	0.93	0.07	0.00
Discomforting pain	0.26	0.59	0.14
Distressing pain	0.00	0.28	0.72
Horrible pain	0.00	0.00	1.00
Excruciating pain	0.00	0.00	1.00
Neuropathic pain (painDETECT score ≤12)	0.10	0.23	0.67
Sensory qualities (SF-MPQ sensory subscale score >10)	0.03	0.46	0.51
Affective qualities (SF-MPQ affective subscale score >1)	0.09	0.33	0.58
Pain catastrophizing (PCS score >5)	0.14	0.40	0.46

Proportions sum across clusters.

Abbreviations

SF-MPQ PPI: McGill Pain Questionnaire (Short Form) Present Pain Intensity; SF-MPQ: McGill Pain Questionnaire (Short Form); PCS: Pain Catastrophizing Scale

FIGURE LEGENDS

Figure 1: Response probabilities of each pain dimension variable, per cluster: cluster one (n=95), cluster two (n=83) and cluster three (n=49).

Response probabilities sum down clusters. Ordinal proportions (GCPS and SF-MPQ PPI) sum to one and are shaded as per legend. Dichotomous variable proportions show proportion above cut-point.

Abbreviations

C1 - Cluster one: Uni-dimensional pain profile; C2 - Cluster two: Moderate multi-dimensional pain profile; C3 - Cluster three: Severe multi-dimensional pain profile; GCPS : Graded Chronic Pain Scale; SF-MPQ PPI: McGill Pain Questionnaire (Short Form) Present Pain Intensity; PCS: Pain Catastrophizing Scale; SF-MPQ: McGill Pain Questionnaire (Short Form)

Figure 2: Risk profile for cluster two and cluster three, compared to cluster one.

Relative risk ratios for continuous variables are expressed per standard deviation decrease for SF-36 quality of life physical and mental component scales, and per standard deviation increase in the variable depression. Regression coefficients at $p < 0.01$ significance are colored blue.
*Relative risk ratio per standard deviation increase.
†Quality of life reverse scored (100-score) i.e. greater risk with lower quality of life.

Abbreviations
RRR: Relative risk ratios; CI: Confidence Interval; BMI: Body Mass Index; QOL: Quality of life; SD: Standard deviation;