Low Back Pain Patient Subgroups in Primary Care

Pain Characteristics, Psychosocial Determinants, and Health Care Utilization

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Objectives: In industrialized countries, low back pain (LBP) is one of the leading causes for prolonged sick leave, early retirement, and high health care costs. Providing the same treatments to all patients is neither effective nor feasible, and may impede patients' recovery. Recent studies have outlined the need for subgroup-specific treatment allocation.

Methods: This is a cross-sectional study that used baseline data from consecutively recruited patients participating in a guideline implementation trial regarding LBP in primary care. Classification variables were employment status, age, pain intensity, functional capacity (HFAQ), depression (CES-D), belief that activity causes pain (FABQ subscale), 2 scales of the SF-36 (general health, vitality), and days in pain per year. We performed k-means cluster analyses and split-half cross-validation. Subsequently, we investigated whether the resulting groups incurred different direct and indirect costs during a 6-month period before the index consultation.

Results: A 4-cluster solution showed good statistical quality criteria, even after split-half cross-validation. "Elderly patients adapted to pain" (cluster 1) and "younger patients with acute pain" (cluster 4) accounted for 55% of all patients. Cluster validation showed the lowest direct and indirect costs in these groups. About 72% of total costs per patient referred to clusters 2 and 3 ("patients with chronic severe pain with comorbid depression" and "younger patients with subacute pain and emotional distress").

Discussion: Our study adds substantially to the knowledge of LBP-related case-mix in primary care. Information on differential health care needs may be inferred from our study, enabling decision makers to allocate resources more appropriately and to reduce costs.

Key Words: low back pain, cluster analysis, health care costs, treatment allocation

(*Clin J Pain* 2014;30:1023–1032)

About 85% of the total health care costs in industrialized countries are caused by work loss due to low back pain (LBP).[1] Despite a high rate of spontaneous recovery, patients have frequent recurrences and about 2% to 7% of patients develop chronic pain.[2] Therefore, back pain management should aim for a symptomatic approach in those patients in whom spontaneous recovery is expected, and an intensified therapy for those who are at risk for chronicity, or who have chronic pain. Psychosocial factors have been shown to influence patients' prognosis,[3] which is why current guidelines recommend using the presence of psychosocial yellow flags to prompt early intervention in nonspecific LBP patients.[4] It seems irrational to administer the same treatment strategies to all patients not only with respect to patient outcomes, but also for economic reasons. Evidence on the effectiveness of different treatment strategies is increasing, and some main treatment pathways exist, such as patient counseling to enhance activity, drug treatment for pain relief, and multimodal therapy for those at risk for chronicity or with chronic LBP (CLBP).

Psychosocial factors have been investigated in studies using prognostic screening instruments. Haldorsen et al[5] developed a prognosis score for long-term sick-listed employees with musculoskeletal pain. Three groups of patients with good, medium, and poor prognoses were then randomized to treatments of different intensities. Haldorsen and colleagues showed that patients with a poor prognosis receiving extensive multidisciplinary treatment were more likely to return to work than patients with a poor prognosis receiving ordinary treatment. Hill et al[6] presented the Keele STarT Back Screening Tool as a short primary care questionnaire developed to stratify treatment based on a low, medium, and high psychosocial risk in LBP patients. Similar to Haldorsen's study, the authors found small but significant effects regarding the outcome of treatment.

Apart from studies designed to identify patients at risk for chronicity and to evaluate differential treatment strategies, there is further research on patterns of patient

Received for publication November 30, 2012; revised January 30, 2014; accepted January 22, 2014.
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Supported by the German Ministry for Education and Research, Berlin, Germany (BMBF, grant number FKZ 01 EM 0113). The authors declare no conflict of interest.
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DOI: 10.1097/AJP.0000000000000080

characteristics that will add to the understanding of setting-specific case mixes and subsequently setting-specific management. In this respect, on the basis of the West Haven-Yale Multidimensional Pain Inventory, 3 homogeneous subgroups were identified: Dysfunctional, Interpersonally Distressed, and Adaptive Copers.[7] Dysfunctional patients had high levels of pain, reduced quality of life, and high levels of emotional distress. Interpersonally Distressed patients shared these issues and also had less support from significant others. The Adaptive Copers had low levels in the areas of pain, functional limitations, and emotional distress. This taxonomy was validated using several external criteria. Further subgroups were formed on the basis of fear and avoidance beliefs, pain catastrophizing, and depression with cluster analysis.[8–10] They were validated by showing differences in health care usage and sick leave.

Another subgrouping approach was based on the avoidance-endurance model combined with emotional distress.[11] Apart from fear-avoidance responses, endurance-related responses in severe pain, together with emotional distress, can lead to chronic pain. Hasenbring et al[12] used a classification tool based on the Avoidance-Endurance Questionnaire and the Beck Depression Inventory to classify patients with subacute nonspecific LBP in primary care. They found distress-endurance, eustress-endurance, and fear-avoidance response patterns, which should be individually targeted with cognitive-behavioral treatments. This model was also evaluated positively in several other validation studies.

Scholz et al[13] were able to differentiate patients with neuropathic pain from patients with non-neuropathic pain. Data from a structured interview and a standardized bedside examination were analyzed with hierarchical cluster analysis and classification tree analysis. The achieved subgrouping was considered to be important in improving targeted analgesic treatment. It was further shown that nonspecific LBP is not a homogeneous condition.[14,15] Patients who were receiving matched treatments showed greater therapeutic success than those receiving unmatched treatments. Therefore, it is important to find practically important subgroupings.

Kent and Keating[16] used survey data to advocate for further research when they noticed a lack of consensus and a lack of evidence regarding LBP subgroups among primary care clinicians. Adequate treatment facilities for subacute and chronic pain are missing in Germany.[17] As in other countries, general practitioners (GPs) are the coordinators of care who play an essential role in effective treatment allocation. To understand consulters' case-mix means to learn more about health care needs and the prevalence of different subgroups; this could be addressed in future effectiveness studies or for the development of subgroup-specific interventions of different intensities. We therefore performed a secondary analysis of a primary care effectiveness trial. The aim was to identify patterns of patient characteristics, pain characteristics, and group-specific health care utilization. On the basis of current evidence, we used a broad spectrum of sociodemographic and psychosocial variables to get a multivariate picture of LBP patients[18] in a primary care setting of consecutively recruited back pain patients.

MATERIALS AND METHODS

Study Design

This is a post hoc analysis of a 3-armed randomized controlled trial with an educational intervention in a primary care setting (guideline implementation, guideline implementation plus motivational counseling, control group with postal dissemination of guideline).[19] The primary goal of the trial was to assess the impact of guideline-oriented treatment on functional capacity in patients with LBP. A predefined secondary goal of the trial was to explore the different use of health care services for LBP. The trial was conducted in 2 centers, Marburg and Göttingen, Germany. As this is a secondary analysis of the trial, all involved researchers were blinded to possible subgroups at baseline while collecting data. Our methods comply with the Declaration of Helsinki. Ethical approval was obtained from both study sites.

All patients and physicians gave their written informed consent. Patients reporting LBP were consecutively recruited. Inclusion criteria were LBP on the day of inclusion, age above 19, and ability to read and understand German. Exclusion criteria were pregnancy and isolated thoracic or cervical pain.

At the index visit, patients were asked to fill out 2 sets of questionnaires, one while waiting and another one at home (returned in a prepaid mailer). A baseline telephone interview was performed within 4 weeks by specially trained clinical nurses. The data from 2 follow-up interviews (after 6 and 12 mo) are not included in this analysis.

GPs evaluated each patient regarding the presence of complicating factors (red flags: being unwell, history of trauma, suspected cancer, major neurological deficits, signs of rheumatic disease, osteoporosis, fever, immune deficiency, or significant trauma) on a 1-page questionnaire. For a more detailed description of the study design please refer to Becker et al.[20,21]

Measurement Instruments

Functional capacity was measured with the Hannover Functional Ability Questionnaire for measuring back pain–related functional limitations (HFAQ). The HFAQ is a 12-item self-administered questionnaire for the assessment of functional limitations in activities of daily living (internal consistency, $\alpha = 0.90$; retest reliability, $r = 0.75$).[22,23] Normal function shows scores of 80% to 100%; scores around 70% equal a moderately limited function; scores below 60% equal a severely limited function.

For the measurement of fear-avoidance beliefs, we utilized the German version of the Fear-Avoidance Beliefs Questionnaire (FABQ)[24] by Pfingsten et al.[25] This questionnaire assesses the cognitive aspect of pain-related fear avoidance on 7-point Likert scales focusing on patients' beliefs about how physical activity and work affect LBP. The German FABQ shows a different factor structure from the original English version. The factor "physical activity" remained the same as in the English version, the second factor of the English version was split into 2 subscales: one related to "work as cause of pain" and the other to "patients' assumptions of their probable return to work." The subscales showed modest to good internal consistencies. In the present context, the subscale "physical activity" (FABQphys; range, 0 to 30) was used to determine the relationship between beliefs and reported physical activity. Pfingsten and colleagues found a Cronbach $\alpha = 0.69$, whereas we calculated a Cronbach $\alpha = 0.73$ in a sample of primary care patients.[26] The other scores were not used in the present analysis as they refer to employment status, and about two thirds of our sample had no paid employment.

Depression was assessed with the German version of the Center for Epidemiologic Studies Depression Scale (CES-D).[27] A score of 23 or more indicates a depressive disorder.[28] For description of pain we asked for the pain intensity (0 to 100 numeric analog scale) and days in pain during the previous year.

Emotional and physical symptoms were measured with the German version of the symptom checklist (SCL-90-R) by Derogatis,[29] a self-report questionnaire to assess different dimensions of psychopathology, like obsessions and compulsions, depression, anxiety, and others. We used the somatization dimension as it is close to physical symptoms like LBP. Health-related quality of life was measured with the EuroQol[30] and the SF-36 Health Survey[31] for general health and vitality. The EuroQol describes present-day health status on 5 dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression on 3-point scales and asks about the actual health state on a visual analog scale (0 to 100). In our study, patients rated their actual health on the visual analog scale. The SF-36 Health Survey consists of the following subscales: physical functioning, role limitations because of physical health problems, bodily pain, social functioning, general mental health, role limitations because of emotional problems, vitality (energy/fatigue), and general health perceptions. In our study we used subscales "vitality" and "general health perceptions" as these are additional aspects affected by LBP.

Measurement of Health Care Utilization

Telephone interviews were conducted to collect data on health care utilization during the 6-month period before the index date. Consultation of health care providers (GP, specialists), diagnostic and therapeutic procedures, and auxiliaries were given in types and numbers referring to a 6-month period before recruitment of patients. For pharmaceuticals, information given by patients was initially translated into drug codes. Data on hospital and rehabilitation were given in days of care and reason for admission (eg, surgery, pain management).

Valuation of Direct and Indirect Costs

All costs were valued for the year 2004 from the societal perspective. As we had no data on insurance status, we postulated a 10% rate of privately insured patients for all direct cost categories. Physician consultations, as well as diagnostic and therapeutic procedures, were priced using provider-specific charges. The costs for drugs were based on package prices according to the official German price list of drugs (Rote Liste). Expenditures for hospital care are based on diagnosis-related groups or on department-specific daily charges, increased for 2004 by the sector-specific and land-specific inflation rate (adopted from classification of individual consumption on purpose—COICOP, Hessen: 21.4%, Niedersachsen: 24.3%).[32] For costs of inpatient rehabilitation, we used sector-specific charges (year 2000, information from regional rehabilitation clinics) inflated for 2004. If necessary, we accounted for patient copayment in all cost categories. Cost estimations for auxiliaries are based on average prices recommended by Krauth et al[33] (inflated for 2004) or by personal information from medical supply stores.

For an estimation of indirect costs we used the human capital approach, multiplying the number of missed work hours with the average daily labor cost in Germany. Persons who were not employed had "0" sick leave days as we looked at this issue from the perspective of direct costs for society. A more detailed description of cost evaluation may be seen in Becker et al.[20]

Statistical Analyses

We performed k-means cluster analyses generalized to all scales of measurement with squared Euclidean distances.[34] The k-means procedure identifies relatively homogeneous subgroups while maximizing the variability between clusters. Variables with mixed scaling can be handled in cluster analysis.[34,35] Calculations were made with ALMO 12 (http://www.almo-statistik.de), which includes a k-means algorithm able to handle the different scaling of our variables and the large sample size. This program provides statistical measures to evaluate the appropriateness of a cluster solution (F value, η^2). The F value is calculated following analysis of variance. It can be regarded as the maximum F value as the variation between clusters is maximized.[35,36] This F_{max} value does not follow an F distribution, in contrast to analysis of variance. Therefore, no test of significance is possible. η^2 represents the effect size in a general linear model (GLM). It is an omnibus effect size when examining the cluster solution as a whole and a partial η^2 when examining the contribution of single variables to the cluster solution. In the latter case, we stated the significance level of the GLM analyses between the clusters on single variables. Post hoc Tukey Honest Significant Difference tests were performed to show which clusters differ on a specific variable. Differences regarding metric variables in health care utilization were analyzed with Kruskal-Wallis tests and post hoc Mann-Whitney U tests as these variables were highly skewed. Differences regarding categorical variables were evaluated with χ^2 tests and the corresponding Cramer V effect size. Cramer V values of 0.40 and higher denote large effects.[37]

We used baseline data from all patients, regardless of group allocation, in our randomized trial because we intended to find groups in patients with LBP before therapeutic interventions. We then investigated whether these groupings differed with respect to direct and indirect costs. Only relevant variables should be included in a cluster analysis. Irrelevant variables can destroy the clustering and prevent an interpretable solution to appear.[36,38] Consequently, cluster analysis is an iterative process. Therefore, we ran several analyses and excluded variables with no meaningful contribution. The exclusion criterion was $\eta^2 < 0.10$.[34] We performed single-sample cross-validation, although this method has some limitations.[39,40] We validated our cluster solution by health care utilization and resulting direct and indirect costs during a 6-month period before study participation.

RESULTS

Study Sample

We contacted 883 GPs; 126 GPs agreed to participate. A total of 69 (55%) practices were run by a single GP. The GPs had been practicing an average of 12.4 years (range, 1 to 31 y); the average age of the GPs was 48 years (SD = 6) (national average, 50.4 y), and 42% of them were female (national average, 36%). In total, 1378 patients were included in the study. Baseline characteristics of the patient sample are depicted in Table 1.

Cluster Analysis

Information on 1200 patients could be used for the analyses as there was missing data. Variables with no

TABLE 1. Baseline Characteristics of the Study Sample (n = 1378)

Demographic characteristics	
Age (mean [range; SD])	48.85 (20-91; 13.7)
Sex (male, n [%])	574 (41.65)
Employment status (n [%])	
No paid work	453 (32.9)
Part-time	357 (25.9)
Full-time	568 (41.2)
Net income per month (n [%])* (in Euros)	
≤1000	199 (14.4)
1001-2000	478 (34.7)
2001-3000	288 (20.9)
>3000	120 (8.7)
Characteristics of LBP	
Functional capacity (mean [SD])	67.45 (21.43)
Pain intensity (NRS 0-100) (mean [SD])	53.87 (17.03)
Days of pain in the previous year (median)	30
Duration of the current episode in days (median)	6
Quality of life (VAS 0-100) (mean [SD])	57.05 (19.27)
Chronic pain grade* (n [%])	
Low disability/low intensity	303 (22.0)
Low disability/high intensity	258 (18.7)
High disability/moderately limiting	260 (18.9)
High disability/severely limiting	164 (11.9)
Red flags (n [%])	
Generally unwell	28 (2.0)
Neurological deficits	20 (1.5)
History of cancer	22 (1.6)
Chronic inflammatory disease	32 (2.3)
Osteoporosis with danger of fracture	29 (2.1)
Fever	2 (0.1)
Immune deficiency	0
Severe trauma	8 (0.6)
Job satisfaction (NRS 0-10) (mean [SD])	6.10 (2.46)
Depression score (mean [SD])	15.36 (9.38)
Proportion of patients scoring ≥23 points on CES-D (%)	15.9
Fear-avoidance beliefs (mean [SD])	
Score I (physical activity = cause of pain)	17.59 (6.80)

* > 20% missing data.
LBP indicates low back pain; NRS, numeric rating scale; VAS, visual analog scale.

meaningful contribution ($\eta^2 < 0.10$) were sex, marital status, education, EuroQol, and symptom checklist (SCL-90-R). The variables used for classification were employment status, age, pain intensity, functional capacity (HFAQ), depression (CES-D), belief that activity causes pain (subscale of the FABQ), 2 scales of the SF-36 (general health, vitality), and days in pain per year. As shown in Table 2, the categories "no paid work" and "full time" of employment status, age, subscales "general health" and "vitality" of the SF-36, and depression (CES-D) contributed most to the cluster solution.

A 4-cluster solution was best interpretable and resulted in an F value of 241.61 and an η^2 of 0.345, meaning that 34.5% of the variance can be explained by this partitioning. Consequently, this cluster solution possesses good quality criteria.[34,38,41,42]

All included variables contributed substantially to the breakdown into 4 clusters. For example, 54.2% of the variance of the category "full time" within the variable "employment status" is explained by the partitioning into 4 clusters. Other prominent variables are age, health status, no paid employment, vitality, and depression.

Table 2 depicts the characterization of the 4 clusters by means and proportions of classification and description variables. It further lists the results of testing for significance between clusters by univariate GLMs and post hoc Tukey Honest Significant Difference tests. The only nonsignificant difference occurred in "activity causes pain" between clusters 1 and 3. Because of high SDs in relation to the means, we list the median of the variable "days in pain."

The mean age of cluster 1 patients is 65 years. Two thirds of these patients have no paid employment. Patients show a medium pain intensity in the preceding 3 months, have a moderate functional capacity, low depression scores, a medium belief that activity causes pain, medium general health and vitality, and a rather high number of days in pain. This cluster can be labeled as "elderly patients adapted to pain."

Cluster 2 comprises a mixed employment status, with equal representation between the 3 categories: having no paid employment, working part-time, working full-time. Members average 56 years of age, have high pain intensity in the preceding 3 months, a low functional capacity, high depression scores, strong beliefs that activity causes pain, low general health and vitality, and a very high number of days in pain. This cluster can be labeled as "chronic severe pain with comorbid depression."

Cluster 3 mainly consists of full-time employees at a younger age with medium pain intensity in the preceding 3 months, moderate functional capacity, increased depression scores, a medium belief that activity causes pain, medium general health, below-medium vitality, and a medium number of days in pain. This cluster can be labeled "younger patients with subacute pain and emotional distress."

Cluster 4 is mainly made up of full-time employees at a younger age with below-medium pain intensity in the preceding 3 months, a high functional capacity, low depression scores, a medium belief that activity causes pain, high general health and vitality, and a low number of days in pain. This cluster can be labeled "younger patients with acute pain."

We performed single-sample cross-validation by the split-half technique. In both subsamples (n = 601 and 599) 4-cluster solutions had the best statistical quality criteria. In the first subsample there was an F value of 128.90 and an η^2 of 0.361, whereas in the second subsample the F value was 117.52 with an η^2 of 0.340. The two 4-cluster solutions after cross-validation are characterized in Table 3.

In the 2 cross-validations there were more nonsignificant differences between clusters compared with that in the original solution, but the general pattern was supported. Exceptions to this are the distributions of employment status in clusters 1 and 2. In the second cross-validation there were more elderly patients in cluster 2 and less of them in cluster 1. Therefore, functional capacity was higher and the belief that activity causes pain was lower in patients in the second cross-validation of cluster 1. The most striking difference to the solution was the lower days in pain in the second cross-validation of cluster 1. More younger people entered cluster 1, and days in pain obviously did not have a high meaning for patients in cluster 1 as they are well adapted to pain.

Cluster-specific Health Care Utilization

As the general patterns in our sample were supported, we performed calculations regarding health care utilization and costs with the 4-cluster solution of the complete sample.

TABLE 2. Characterization of the 4 Clusters of Low Back Pain Patients by Proportions, Means With SDs, and Medians of Classification and Sex (n = 1200)

	Cluster 1 Elderly Patients Adapted to Pain	Cluster 2 Chronic Severe Pain with Comorbid Depression	Cluster 3 Younger Patients With Subacute Pain and Emotional Distress	Cluster 4 Younger Patients With Acute Pain	η^2 and Significance Testing
n (%)	247 (21)	158 (13)	383 (32)	412 (34)	
Classification					
Employment status (%)					χ^2: $P < 0.001$ Cramer $V = 0.57$
No paid work	67	36	1	0	0.49
Part-time	30	32	13	12	0.05
Full-time	3	32	86	88	0.54
Age	65.33 (7.52)	56.12 (12.25)	43.51 (9.36)	40.87 (9.70)	0.50
					GLM: $P < 0.001$
Pain intensity	50.53 (14.63)	72.69 (14.49)	55.95 (14.32)	44.39 (14.55)	0.28
					GLM: $P < 0.001$
Functional capacity (HFAQ)	67.74 (17.66)	42.75 (16.52)	63.43 (19.30)	79.24 (18.52)	0.28
					GLM: $P < 0.001$
Depression (CES-D)	11.97 (6.68)	24.60 (9.58)	19.80 (9.13)	9.95 (5.69)	0.34
					GLM: $P < 0.001$
Activity causes pain (FABQ)	17.82 (7.38)	22.85 (5.29)	18.14 (5.78)	14.94 (6.52)	0.13
	NS		NS		GLM: $P < 0.001$
Quality of life (SF-36)					
General health	55.02 (12.59)	34.77 (12.30)	50.33 (13.37)	71.75 (11.34)	0.50
					GLM: $P < 0.001$
Vitality	53.39 (14.34)	30.36 (14.50)	40.29 (12.72)	62.48 (13.81)	0.42
					GLM: $P < 0.001$
Days with pain (median)	90	356	40	20	0.27
					GLM: $P < 0.001$
Description					
Female (n [%])	147 (59.5)	103 (65.6)	222 (57.8)	223 (54.1)	

Contribution of classification variables to the 4-cluster solution (η^2) and testing for significance between clusters by univariate general linear models (GLM) and post hoc Tukey Honest Significant Difference tests.

NS indicates nonsignificant comparisons with post hoc Tukey Honest Significant Difference tests, all other pairwise comparisons $P < 0.02$.

In cluster 1 the elderly patients who are adapted to pain have a high intake of nonsteroidal anti-inflammatory drugs (NSAIDs). Cluster 2, which also includes elderly patients who are not adapted to pain, has the highest direct and indirect annual costs (high GP consultation rate, high intake of opioids, high number of physiotherapy sessions, high rate of sick leave, and the highest number of days in hospital or rehabilitation). The second highest direct and indirect costs can be found in cluster 3, which mainly consists of younger patients with subacute pain and emotional distress (high number of orthopedic consultations, high intake of NSAIDs, high rate of imaging tests, high number of days in hospital and rehabilitation care, and a high number of physiotherapy sessions). Annual costs of patients in cluster 4 almost equal those of patients in cluster 1, but the younger patients with acute pain in cluster 4 have lower direct and indirect costs (less GP consultations or orthopedic and pain specialist consultations, lower numbers of NSAIDs, opioids, imaging tests, sick leave, days in hospital, or of physiotherapy sessions [Tables 4 and 5]).

DISCUSSION

Our aim was to find subgroups in cross-sectional data of LBP patients in general practice that are likely to need a specific treatment.[43] After identifying subgroups, we tried to validate them with health care utilization and costs, which has to be characterized as a narrow form of validation on the same sample. This approach can be regarded as hypothesis-setting as it generates hypotheses about potential treatment-effect modifiers. Our subgroups were data-driven on the basis of statistical analyses with the unsupervised technique of cluster analysis.

We performed a k-means cluster analysis on a large data set of primary care patients with LBP. We found 4 clusters that were stable, even after split-half cross-validation, and can be characterized as "elderly patients adapted to pain" (cluster 1), "patients with chronic severe pain and comorbid depression" (cluster 2), "younger patients with subacute pain and emotional distress" (cluster 3), and "younger patients with acute pain" (cluster 4). Patients in clusters 2 and 3 accounted for 72% of total health care cost, arising from almost equal proportions of high direct and indirect costs.

In light of the ongoing discussion on relevant patient subgroups with LBP, cluster analysis could be a suitable technique to take into account the complexity of pain, but its results are dependent on the input of variables. Our 2 clusters, "patients with chronic severe pain with comorbid depression" and "younger patients with subacute pain and emotional distress," resemble patients with chronic pain and those at risk for chronicity who are addressed in current guidelines.[44,45] According to these recommendations they should be identified by the persistence of pain and/or

TABLE 3. Characterization of the 4-Cluster Solutions After Split-half Cross-validation (1 and 2) by Proportions, Means With SDs, and Medians of Classification Variables and Sex (n = 1200)

	Cluster 1 Elderly Patients Adapted to Pain	Cluster 2 Chronic Severe Pain With Comorbid Depression	Cluster 3 Younger Patients With Subacute Pain and Emotional Distress	Cluster 4 Younger Patients With Acute Pain	η^2 and Significance Testing
n (%)					
1 (n = 601)	131 (22)	77 (13)	184 (30)	209 (35)	
2 (n = 599)	108 (18)	96 (16)	200 (33)	195 (33)	
Classification					
Employment status (1/2) (%)					
No paid work	67/49	36/56	1/1	0/0	(1) χ^2: $P < 0.001$ Cramer $V = 0.58$ (2) χ^2: $P < 0.001$ Cramer $V = 0.58$
Part-time	30/48	31/27	9/14	10/9	
Full-time	3/3	33/17	90/85	90/91	
Age					
1	65.13 (8.25)	57.47 (12.49)	43.79 (9.41)	40.08 (10.02)	0.51 GLM: $P < 0.001$
2	62.24* (8.40) NS*	59.95* (11.13) NS*	42.97† (9.53) NS†	41.17† (8.97) NS†	0.48 GLM: $P < 0.001$
Pain intensity					
1	51.89 (15.76)	74.47 (13.35)	58.30 (14.61)	42.42 (14.87)	0.33 GLM: $P < 0.001$
2	46.28* (13.06) NS*	67.17 (15.15)	55.26 (14.26)	45.86* (13.73) NS*	0.23 GLM: $P < 0.001$
Functional capacity (HFAQ)					
1	65.86* (18.19) NS*	41.23 (15.86)	60.97* (19.47) NS*	80.77 (16.31)	0.34 GLM: $P < 0.001$
2	74.05*(15.07) NS*	46.11 (17.57)	65.74 (18.68)	76.79* (21.18) NS*	0.24 GLM: $P < 0.001$
Depression (CES-D)					
1	11.80 (6.77)	24.42 (10.00)	20.85 (10.09)	11.38 (5.87)	0.29 GLM: $P < 0.001$
2	11.71 (6.35)	20.70* (9.73) NS*	19.79* (8.57) NS*	8.73 (5.36)	0.33 GLM: $P < 0.001$
Activity causes pain (FABQ)					
1	18.11* (7.18) NS*	23.30 (5.48)	18.46* (5.95) NS*	14.35 (6.17)	0.17 GLM: $P < 0.001$
2	15.70* (7.78) NS*	22.43 (5.22)	18.04 (5.52)	15.84* (6.66) NS*	0.12 GLM: $P < 0.001$
Quality of life (SF-36)					
General health					
1	55.49*(12.75) NS*	32.18 (11.69)	51.96* (13.15) NS*	70.81 (12.42)	0.47 GLM: $P < 0.001$
2	57.68 (11.76)	40.55 (12.84)	47.56 (14.09)	72.52 (10.85)	0.50 GLM: $P < 0.001$
Vitality					
1	54.63 (15.31)	28.47 (13.76)	40.00 (13.50)	61.58 (13.90)	0.41 GLM: $P < 0.001$
2	55.28 (13.37)	36.56* (13.91) NS*	38.85* (12.44) NS*	63.26 (13.74)	0.43 GLM: $P < 0.001$
Days with pain (median)					
1	100	365	40	14	0.31 GLM: $P < 0.001$
2	12* NS*	340	60	20* NS*	0.33 GLM: $P < 0.001$
Description					
Female (%)					
1	62.6	67.5	55.4	52.2	
2	56.5	59.0	56.9	58.4	

Contribution of classification variables to the 4-cluster solution (η^2) and testing for significance between clusters by univariate general linear models and post hoc Tukey Honest Significant Difference tests.

* and † Nonsignificant pairwise comparisons.

NS indicates nonsignificant comparisons with post hoc Tukey Honest Significant Difference tests, all other pairwise comparisons $P < 0.01$.

TABLE 4. Health Care Utilization in Clusters

	Cluster 1 Elderly Patients Adapted to Pain n = 247	Cluster 2 Patients With Chronic Severe Pain With Comorbid Depression n = 158	Cluster 3 Younger Patients With Subacute Pain and Emotional Distress n = 383	Cluster 4 Younger Patients With Acute Pain n = 412	
GP consultations					
≤1	64 (25.9)	22 (14.0)	106 (27.7)	157 (38.1)	χ^2: $P < 0.001$ Cramer $V = 0.22$
2-5	119 (48.2)	44 (28.0)	191 (49.9)	206 (50.0)	
6-10	36 (14.6)	40 (25.5)	36 (9.4)	32 (7.8)	
> 10	24 (9.7)	45 (28.7)	38 (9.9)	4 (1.0)	
Orthopedics	70 (28.3)	78 (49.7)	124 (32.4)	103 (25.0)	χ^2: $P < 0.001$ Cramer $V = 0.17$
Pain specialist	11 (4.5)	14 (8.9)	13 (3.4)	7 (1.7)	χ^2: $P = 0.001$ Cramer $V = 0.12$
Psychotherapist	6 (2.4)	8 (5.1)	16 (4.2)	7 (1.7)	χ^2: $P = 0.08$ Cramer $V = 0.08$
Oral medication					
Analgesics	15 (6.1)	17 (10.8)	27 (7.0)	18 (4.4)	χ^2: $P = 0.04$ Cramer $V = 0.08$
NSAID	142 (57.5)	82 (52.2)	186 (48.6)	189 (45.9)	χ^2: $P = 0.03$ Cramer $V = 0.09$
Opioids	11 (4.5)	36 (22.9)	22 (5.7)	13 (3.2)	χ^2: $P < 0.001$ Cramer V = 0.25
Antidepressants	0	8 (5.1)	2 (0.5)	1 (0.2)	χ^2: $P < 0.001$ Cramer V = 0.17
Imaging tests (radiology, MRI, CT)	75 (30.4)	71 (45.2)	123 (32.1)	91 (22.1)	χ^2: $P < 0.001$ Cramer $V = 0.16$
Period of (ambulatory/ stationary) rehabilitation (d) (mean [SD])	0.44[1,2] (3.09)	3.2[1,3,4] (9.04)	1.59[2,3,5] (6.69)	0.2[4,5] (1.96)	Kruskal-Wallis: $P < 0.001$ *U* test: 1, $P < 0.001$ 2, $P = 0.02$ 3, $P = 0.02$ 4, $P < 0.001$ 5, $P < 0.001$
median	0	0	0	0	
Period of hospitalization (d) (mean [SD])	0.28[1] (2.09)	0.89[1,2] (4.33)	0.66[3] (3.38)	0.12[2,3] (1.33)	Kruskal-Wallis: $P = 0.001$ *U* test: 1, $P = 0.02$ 2, $P < 0.001$ 3, $P = 0.002$
median	0	0	0	0	
Physiotherapy sessions (mean [SD])	4.36[1,2] (10.17)	6.78[1,3] (10.83)	5.52[2,4] (9.10)	2.62[3,4] (5.9)	Kruskal-Wallis: $P < 0.001$ *U* test: 1, $P = 0.002$ 2, $P = 0.004$ 3, $P < 0.001$ 4, $P < 0.001$
median	0	0	0	0	
Sick leave (d) (mean [SD])	1.64[1,2,3] (13.40)	22.97[1] (50.09)	10.08[2,4] (25.56)	3.62[3,4] (6.73)	Kruskal-Wallis: $P < 0.001$ *U* test: 1, $P < 0.001$ 2, $P < 0.001$ 3, $P < 0.001$ 4, $P = 0.008$
median	0	0	0	0	

Results are given in n (%), if not stated otherwise. Percentages refer to columns excluding missing data for the respective items (valid percentages). CT indicates computed tomography; GP, general practitioner; MRI, magnetic resonance imaging; NSAID, nonsteroidal anti-inflammatory drug.

TABLE 5. Means and Bootstrapped 95% Confidence Intervals of Direct, Indirect, and Total Costs Per Patient in the 4 Clusters (in Euros)

	Cluster 1 Elderly Patients Adapted to Pain n = 247	Cluster 2 Chronic Severe Pain With Comorbid Depression n = 158	Cluster 3 Younger Patients With Subacute Pain and Emotional Distress n = 383	Cluster 4 Younger Patients With Acute Pain n = 412
Direct costs	523.06 (412.5, 722.9)	1411.47 (1089, 1859)	888.95 (721.9, 1112.6)	269.76 (220.0, 359.1)
Physician consultations	81.88 (71.29, 108.75)	114.31 (94.0, 158.4)	93.34 (73.88, 130.56)	49.33 (44.33, 61.52)
Drugs	50.45 (33.71, 86.40)	148.84 (101.0, 244.7)	32.77 (25.00, 47.61)	15.15 (12.98, 18.16)
Diagnostic procedures	83.77 (58.32, 118.51)	161.79 (117.2, 220.6)	113.76 (84.7, 155.9)	40.22 (26.72, 60.08)
Therapeutic procedures	167.33 (136.3, 214.2)	338.67 (272.4, 437.3)	240.07 (202.3, 325.5)	106.12 (90.5, 126.0)
Aids	24.73 (15.36, 38.96)	40.45 (25.11, 67.38)	19.28 (12.71, 28.63)	6.84 (3.977, 11.951)
Hospital care	72.44 (20.95, 192.58)	268.31 (116.7, 549.5)	209.78 (119.4, 346.4)	31.22 (6.29, 102.08)
Rehabilitational care	42.45 (14.13, 95.28)	339.11 (205.9, 534.6)	179.96 (114.4, 271.6)	20.88 (5.94, 53.63)
Indirect costs	124.70 (46.4, 401.4)	1757.63 (1201, 2497)	880.92 (690.9, 1135.8)	354.41 (286.8, 421.7)
Total costs	647.76 (488.2, 955.8)	3169.09 (2448, 4100)	1769.87 (1456, 2188)	615.16 (524.4, 751.8)

yellow flags in order to initiate a more intensified treatment with multimodal interventions, including psychotherapy. Our analysis gives a better understanding of the prevalence of these subgroups with respect to sociodemographical, pain-related, and behavioral characteristics. Our cost data seem to support an increased supply of health care, but costs for rehabilitation and in-hospital care (reflecting utilization of multimodal therapy) and costs for psychotherapy are comparably low. This underlines the suggested undersupply of multimodal therapy in Germany.[17]

Reviewing recent subgroup analyses, repeatable patterns seem to emerge from the data revealing at least 3 consistent subgroups. Two are typically high-risk groups: patients with high impairment and emotional distress (often declared as patients with chronic pain), and patients with less severe disease presentation who are less distressed with lower impairment, but have intense pain. A third group usually refers to patients at low risk for chronicity, including those patients with low levels of pain, impairment, or emotional distress.[8,46,47] Similar to our study, other cluster analyses underline the importance of disability and mood in building patient subgroups. The 2 high-risk groups resemble our clusters 2 and 3. Shaw et al[47] described a low expectation that these groups would return to work, which is not true for our cluster 3. Boersma and Linton,[8] who called these high-risk groups "distressed-fear avoidant" and "fear-avoidant," outlined large percentages of sick leave in these patients, especially in those who are most distressed. This is also consistent with our results of health care utilization showing indirect costs to be highest in cluster 2, which shows a high score of depression, and in cluster 3, in which emotional distress is still an important characteristic. Forty-five percent of our primary care patients belong to the 2 high-risk groups. Boersma and Linton,[8] who also examined primary care patients, found a prevalence of 40%.

The important association between activity patterns and emotional distress was examined in several studies. McCracken and Samuel[48] found 4 distinct activity patterns among individuals with chronic pain with cluster analysis. Their 4 groups showed different levels of avoidance, pacing, and confrontation. Avoidance was associated with greater physical disability and distress and was the most important process regarding daily functioning. Another study examined activity-related behavior among patients with CLBP.[49] A lower activity level for avoiders was not confirmed. Instead, in the subgroup of persisters a higher activity level was associated with an increase of pain, which led to higher distress.

A study of Arnow et al[50] showed that patients with a major depressive disorder and disabling chronic pain had higher costs than patients with depression or pain alone, or those with depression and nondisabling pain. This leads to the conclusion that our patients in cluster 3 need additional treatment for their depressive symptomatology.

Ozguler et al[51] present another study revealing a 4-cluster solution. Differences compared with our clusters mainly relate to patients' age and sex. However, their study included patients with LBP at work. Similar to the study by Ozugler and colleagues, other cluster analyses often examined younger people who were still integrated in the workforce.[8,46,47] This most likely explains differences in the 2 low-risk groups, which, in our analysis, refer to (1) a high age group with pain-related impairments, but reasonable quality of life, and (2) the younger age group with acute pain. Instead, Boersma and Linton[8] described a low-risk group with a depressed mood and a "low-risk" group with lowest scores of pain intensity, depression, and fear avoidance. Future studies including elderly patients need to show whether our postulated association with age will be consistent in different studies. A recent analysis on patients with long-term spinal pain in outpatient and inpatient rehabilitation centers looked for subgroups derived from the Multidimensional Pain Inventory.[52] The authors described 3 subgroups of chronic pain patients: dysfunctional patients, interpersonally distressed patients, and adaptive copers. Because of the different settings and measurements, it is difficult to compare the results of our study with those of Bergström et al.[52] However, focusing on our patients with prolonged pain (clusters 1 to 3) leads one to suspect that there are similarities between the 2 studies with respect to patients' adjustment to pain.

None of the aforementioned studies referred to health care utilization data for cluster validation. Analyses of claims data in the United States revealed a higher comorbidity of LBP patients regarding depression, anxiety, and sleep disorder. Furthermore, they received more pharmacotherapy related and not related to their pain symptoms.[53] Health care costs were significantly higher in LBP patients as they had higher rates of health care utilization. Total direct medical costs were estimated at $8386 (€6529) ± $17,507 (€13,631) in the CLBP group and $3607 (€2808) ± $10,845 (€8444) in the control group. Another US study based on claims data found similar numbers[54] ($7211 [€8525] vs. $2382 [€2816]). The authors further found out that aggressive and costly interventions were performed early in the process of the disorder, contrary to guidelines. In the United Kingdom, direct costs of patients with LBP in primary care were at least twice as high compared with a control group (£1074 [€1269] vs. £516 [€610]).[55] Our results are between those in the United Kingdom and the United States, which points to differences in health care systems.

Our high-risk clusters 2 and 3 account for 72% of total costs. This and the observed proportions of direct and indirect cost within clusters 2 and 3 are in accordance with a study by Wenig et al.[56] In light of the observed pain characteristics, conclusions may be drawn regarding the impact of cluster-specific treatment strategies. Cost savings will be highest when focusing current treatment efforts on clusters 2 and 3. Psychotherapy might be necessary for both groups. Patients with chronic pain seem to need additional treatment modules, which aim to improve disability, fear-avoidance behavior, and quality of life as provided by interdisciplinary rehabilitation. Improving access to multimodal treatment facilities for those patients with chronic pain and to psychotherapists for patients who are emotionally distressed will most likely induce substantial cost savings. Nevertheless, systematic reviews and guidelines found moderate to low evidence for psychological interventions in multidisciplinary rehabilitation programs for patients with CLBP.[57–59] There is a lack of recommendations for patient subgroups, which is also caused by a lack of reliable subgroupings in this area. Therefore, a multivariable approach has to be taken into account when an appropriate treatment program should be tailored to specific patients.[18]

There are limitations to our study. The study results are based on a secondary analysis of a randomized controlled trial and therefore have to be interpreted with caution. Regarding external validity, a selection bias may be present because physicians and patients participating in research studies may be different from those who refuse participation. Physicians could be more interested in evidence-based care, influencing cost data of the study, and patients could be different in pain characteristics, psychosocial data, or health care utilization. It remains unclear in which direction this bias would change the observed associations.

Cost data in our study are gained by retrospective interviews. We cannot exclude recall bias, information bias (eg, by patients who are unable to distinguish between LBP-related procedures and others), or social desirability bias. Underestimation or overestimation of costs is possible. We studied the costs of LBP in primary care from a societal perspective. Total costs are most likely underestimated, because we had to restrict interviews to key issues for practical reasons. For a valuation of physician contacts we followed the recommendations from Krauth et al.[33] These authors based their calculation on assumptions about standard operating procedures instead of detailed patient questioning, which only allows an approximation of costs and may result in their overestimation or underestimation.

A strength of our study is the large sample size. With such a large sample size and a split-half cross-validation, the results of our k-means cluster analysis can be regarded as quite stable.[34]

Our cluster analysis revealed 4 subgroups of LBP patients. Two of these show high scores of disability and high scores of depression or fear avoidance. Intensified therapy as suggested by current guidelines in patients with chronic pain, or in those with persistent pain and yellow flags, could most likely result in substantial cost savings, addressing nearly 45% of back pain patients in primary care. Future research should focus on the cost-effectiveness of subgroup-specific intervention strategies.

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