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ORIGINAL REPORT

DETERMINANTS OF MAJOR DIRECT MEDICAL COST CATEGORIES AMONG PATIENTS WITH OSTEOPOROSIS, OSTEOARTHRITIS, BACK PAIN OR FIBROMYALGIA UNDERGOING OUTPATIENT REHABILITATION

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Objective: **To identify determinants of direct medical costs among patients with osteoporosis, osteoarthritis, back pain or fibromyalgia.**
Design: **Cross-sectional study.**
Participants: **Convenience sample of 410 patients undergoing outpatient rehabilitation.**
Methods: **Resource use was assessed with a self-report retrospective questionnaire, and direct medical costs were calculated considering outpatient physician services, non-physician health services, medication and inpatient treatment. Non-parametric bootstrap techniques with 1,000 replications were used to estimate means of costs and their 95% confidence intervals (CI). To identify determinants of costs, a generalized linear model with log link function and gamma distribution, as well as a multivariate logistic regression analysis, were performed.**
Results: **Medical indication ($p < 0.001$), age ($p = 0.034$) and the scales of the Short Form-36 (SF-36) role physical ($p < 0.001$), physical functioning ($p = 0.036$), social functioning ($p = 0.047$) and vitality ($p = 0.005$) were significant predictors of direct medical costs, whereas the medical indication fibromyalgia (odds ratio (OR) = 5.74, 95% CI 2.051–16.066, $p = 0.001$), the Short-Form 36 (SF-36) scale role physical (OR = 0.988, 95% CI 0.980–0.996, $p = 0.002$) and comorbidity (OR = 1.161, 95% CI 1.043–1.292, $p = 0.006$) were statistically significant determinants of high direct medical costs beyond the median.**
Conclusion: **Our work confirms known predictors of direct medical costs and broadens the understanding of determinants of direct medical costs beyond the median.**

Key words: healthcare costs; direct service costs; musculoskeletal diseases.

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INTRODUCTION

Due to significant limitations in functioning, the economic burden related to musculoskeletal chronic diseases is substantial, and the impact of these disorders on patients and on society is expected to increase dramatically (1, 2). In a recent health survey targeting the burden of diseases across chronic conditions, the impact of disorders such as osteoarthritis (OA), low back pain, fibromyalgia and osteoporosis was considered comparable to the impact of major diseases such as cardiac conditions (3).

An in-depth understanding of the determinants of the economic burden related to the medical treatment of musculoskeletal diseases is the prerequisite to develop tailored cost-saving rehabilitative interventions, and should target both the determinants of direct and indirect costs. In musculoskeletal disorders indirect costs are usually predominant and greater than direct costs due to productivity loss costs (1). However, for lifelong musculoskeletal disorders, such as osteoarthritis, osteoporosis or low back pain, which affect a considerable number of older and already retired persons, as well as for patient populations with high health resource consumption, such as fibromyalgia patients, the use and, more specifically, the high use of healthcare services and the resulting direct costs are of concern for public health policy-makers (4).

During the last decade, many studies have attempted to identify determinants of direct costs among patients with chronic musculoskeletal conditions. Patient-oriented outcomes measured by health-related quality of life (HRQoL) instruments were relevant predictors across musculoskeletal conditions. In rheumatoid arthritis (RA) the Health Assessment Questionnaire (HAQ) was consistently an important predictor of direct costs (4–9). In addition to the HAQ comorbidity, sociodemographic characteristics (10) and the mental health scale of the Medical Outcomes Study Short Form-36 (SF-36) (11) were identified as predictors. In fibromyalgia the number of comorbidities and the fibromyalgia disability, measured with the Fibromyalgia Impact Questionnaire (FIQ), were significant determinants of direct costs (8, 12). In addition, one study among fibromyalgia patients identified not only comorbidity and disability, but also health status, disease severity, perceived self-efficacy, depression and social support as predictors of direct costs beyond the median (13). In OA the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) stiffness, duration of disease and gender were determinants of out-of-pocket expenditures (14), while poorer scores in the dimensions of the SF-36 were a major determinant of direct costs (15). A study targeting specifically the impact of HRQoL instruments on future healthcare resource use in patients with RA and OA also concluded that SF-36, HAQ as well as the WOMAC were all strong predictors of future healthcare resource consumption (4).

However, there is a lack of studies aiming to identify the determinants of direct costs among patients with osteoporosis or back pain and few studies specifically targeted determinants of high direct costs (beyond the median) among patients with chronic musculoskeletal disorders (9, 13). Yet, the understanding of determinants of high direct medical costs across medical conditions is of major importance regarding the development and implementation of efficient rehabilitative interventions. Efficient interventions should aim not only for improvements in functioning, but also for a reduction in high and avoidable direct medical costs. Since such interventions can be developed only if the target population is clearly defined, the identification of subjects at risk of incurring high, and potentially avoidable, direct medical costs is essential.

The objective of this economic evaluation is the identification of determinants of direct medical costs among patients with osteoporosis, OA, back pain and fibromyalgia undergoing outpatient rehabilitation. The specific aims of this work are: (*i*) to explore whether determinants of the distribution of direct medical costs reported in the literature can be confirmed in our work; and (*ii*) to identify determinants of high and potentially avoidable direct medical costs in our population.

MATERIAL AND METHODS

Study design

The present evaluation was performed alongside 2 cohort studies including patients with medical indications of fibromyalgia, OA, osteoporosis or back pain undergoing either daycare or outpatient rehabilitation at the Department of Physical Medicine and Rehabilitation of the University Hospital Munich. Fibromyalgia patients took part in a cohort study targeting the effect of a psychological group intervention on patient's locus of control (data not published, data collection from October 2002 to April 2003). OA, osteoporosis and back pain subjects took part in a prospective cohort study targeting the feasibility of the willingness-to-pay methodology for health effects (data collection from the first quarter of 2003 to the first quarter of 2005) (16). The study population has been described in detail elsewhere (17).

Outcome measures

The unifying framework of concepts and terminology proposed by the International Classification of Functioning, Disability and Health (ICF) was used as a basis for the selection of measures (18). The ICF comprehensively covers all aspects of functioning, which encompasses body structures, body functions, activities and participation and is viewed in relation with the health condition, personal and environmental factors (19).

Resource consumption was assessed with a self-report retrospective questionnaire to collect health resource use (20). In order to cover health condition extensively we collected data about comorbidity using the Self-administered Comorbidity Questionnaire (SCQ) (21). In order to cover body functions as well as activities and participations we used the 8 scales (physical functioning, role physical, bodily pain, general health perception, vitality, social functioning, role emotional, mental health) of the SF-36 (22). In order to cover personal factors, demographic data was collected. Patients answered all questionnaires at the beginning of outpatient rehabilitation.

Direct medical costs

Cost categories considered to calculate direct medical costs were outpatient physician services, non-physician health services, medication and inpatient treatment. These categories were already identified as being major direct medical cost categories in patients with fibromyalgia, OA, osteoporosis or back pain (17). Costs related to outpatient rehabilitation were not included in the analysis. Resource use volumes were combined with unit costs to obtain a net cost per patient. Since recall periods in the self-report retrospective questionnaire to collect health resource use varied from the past 4 weeks (outpatient physician services, non-physician health services, and medication) to the whole research period (inpatient treatment), net costs were extrapolated to obtain annual figures. Medication was evaluated on the basis of prices in the online German drugs index book (23). All other index costs were proposed by the Working Group Methods in Health Economic Evaluation (AG MEA) (24–26). These index costs were extrapolated for 2004 using a factor of 0.025 for the first year and 0.020 for the following years. All costs were calculated in Euros for the year 2004. Due to the skewed distribution of cost data, we used non-parametric bootstrap techniques with 1,000 replications to estimate means of costs and their 95% bias corrected and accelerated confidence intervals (95% CI). Missing cost data was not imputed.

Determinants of direct medical costs and statistical analysis

To identify the determinants of direct medical costs we used two approaches. In order to address determinants of the distribution of direct medical costs a generalized linear model (GLM) with log link function and gamma distribution was performed. GLM have been recommended to be used in multivariate regression analysis of cost data because they provide parametric methods of analysis, whereby a variety of non-normal distributions can be specified and the way covariates act can be altered (27, 28). The Aikake Information Criterion (AIC) and the Pseudo-R^2 were used to select the best model and to address the explanatory power of the final model, respectively. In addition, in order to gather a more meaningful interpretation of direct costs a logistic regression analysis was performed. Due to the usual skewed distribution of costs a suitable, meaningful and current cut-off to dichotomize direct medical costs into high vs low costs is the median of the known distribution (9, 13, 29). Direct medical costs of more than €1,333 (median) were therefore defined as the outcome. A model including all variables of the final GLM model and a final model using backwards selection were estimated. The area under the receiver-operating characteristics (ROC) curve was used to assess model accuracy in discriminating between high and low costs.

The variable selection process included variables comprehensively assessing functioning. Health condition (medical indication, comorbidities), personal factors (age, education level, sex, living with a partner, SF-36 general health perception), body functions (SF-36 scales mental health, vitality and pain), activities and participations (work force participation, SF-36 scales physical functioning, role physical, role emotional and social functioning), and an environmental factor (type of rehabilitation care received) were considered. The correlation of each variable with costs was investigated in univariate analysis. Variables with a *p*-value lower than 0.25 were selected for further analysis. In a second step, a linear regression was performed in order to identify multicollinearity. A Variance Inflation Factor (VIF) higher than 2.5 was considered an indicator of multicollinearity. In order to guarantee the comparability of both regression models the evidence of a significant effect of an independent variable on costs either in the univariate GLM regression or in the univariate logistic regression was a criterion for including the variable in both regression models. In both regression analyses the significance threshold was set at 0.05.

Statistical calculations were performed using the SPSS version 14.0 and the SAS version 9.1.

RESULTS

The characteristics of the 410 patients included in the study are described in Table I. Complete direct medical cost data was available for 72.16% of OA, 72.45% of osteoporosis, 72.73% of back pain and 77.78% of fibromyalgia patients. The data-set

Table I. *Characteristics of the sample*

Variables	Osteoarthritis	Osteoporosis	Back pain	Fibromyalgia	Total
Total number, *n*	97	98	143	72	410
Sex, female, *n* (%)	66 (68)	83 (84.7)	97 (67.8)	72 (100)	318 (77.6)
Age, years, mean (SD)	66.56 (10.53)	66.85 (7.63)	52.91 (14.22)	53.49 (8.62)	59.57 (13.00)
Subjects living in partnership, *n* (%)	52 (53.6)	49 (50.0)	84 (58.7)	50 (69.4)	235 (57.3)
Subjects with high educational level, *n* (%)	36 (37.1)	34 (34.7)	70 (49.0)	10 (13.9)	150 (36.6)
Subjects with paid work, *n* (%)	15 (15.46)	8 (8.16)	68 (47.55)	35 (48.6)	126 (30.73)
Retired, *n* (%)	61 (62.9)	66 (67.3)	29 (20.3)	17 (23.6)	173 (42.2)
Comorbidity score (SCQ), mean (SD)	3.69 (2.43)	5.23 (2.94)	2.33 (2.74)	6.26 (3.52)	4.06 (3.23)
SF-36 Physical score, mean (SD)	31.97 (8.47)	37.19 (9.38)	34.86 (8.99)	30.40 (6.59)	33.96 (8.91)
SF-36 Mental score, mean (SD)	49.26 (10.42)	50.25 (9.58)	48.95 (10.69)	40.03 (12.28)	47.85 (11.18)

SF-36: Short-Form 36; SD: standard deviation; SCQ: Self-administered Comorbidity Questionnaire.

was complete regarding sex, age, medical indication and treatment, but values were missing (percentage of missing values) considering educational level (7.6%), participation at the work force (6.1%), comorbidity score (7.3%) and the SF-36 scales (between 7.85% and 10.2%). Since subjects with complete data-sets ($n = 275$) did not statistically significantly differ from subjects without complete data-sets ($n = 135$) regarding age, sex, educational level, participation at the work force and the comorbidity score, missing values can be supposed to be missing completely at random. However, multiple imputation techniques could not be used adequately due to the absence of high correlated covariates. The bias introduced by inadequately imputing missing data was therefore considered to be worse than the loss of power introduced by restricting the analysis to those observations with complete data. Hence, solely the 275 subjects (67%) with complete data were considered in the regression analysis.

Direct medical costs and their components are displayed in Table II. The univariate regression analyses are presented in Table III. Neither the univariate GLM regression nor the univariate logistic regression showed any evidence that sex, living with a partner and treatment should be included in the final models.

The final multivariate GLM model and a logistic regression model including the same variables are presented in Table IV. In the final GLM regression model medical indication, age and the scales of the SF-36 role physical, physical functioning, social functioning and vitality were statistically significant predictors of direct medical costs.

The explanatory power (Pseudo-R^2) of the final GLM model was estimated to be 32.87%. In the final logistic regression model the medical indication fibromyalgia (OR = 5.74, 95% CI 2.051–16.066, $p = 0.001$), the SF-36 scale role physical (OR = 0.988, 95% CI 0.980–0.996, $p = 0.002$) and comorbidity (OR = 1.161, 95% CI 1.043–1.292, $p = 0.006$) were statistically significant determinants of high direct medical costs. The probability (estimated with ROC curves) that the final logistic model can correctly distinguish between low and high cost was estimated to be approximately 76.4%.

DISCUSSION

We found that age, medical condition, comorbidities and various aspects of quality of life may explain direct medical costs. Our results are largely consistent with the determinants identified in previous studies examining the direct medical costs of single conditions. In addition, our work is the first to show in a direct comparison the magnitude of the economic burden related to fibromyalgia.

An important aspect of our work was the examination of the determinants of high medical costs as defined beyond the median (€1,333), which is a suitable, meaningful and current cut-off used to dichotomize direct medical costs (9, 13, 29). Differing from the analysis of direct medical costs using linear regression modelling, we found that comorbidity seems to play an important role and may in fact be more important than some additional aspects of physical functioning beyond role

Table II. *Cost components and annual direct medical costs before rehabilitation. Values are means (95% bias accelerated and corrected confidence intervals) calculated with 1,000 bootstrap samples. All values in Euros*

	Osteoarthritis ($n = 97$)	Osteoporosis ($n = 98$)	Back pain ($n = 143$)	Fibromyalgia ($n = 72$)	Total ($n = 410$)
Outpatient physician visits	356.77 (259.92; 458.94)	262.66 (185.88; 333.12)	547.35 (384.05; 727.65)	1,438.83 (1065.44; 1846.27)	607.72 (499.16; 718.46)
Non-physician services	170.71 (121.90; 226.78)	257.61 (160.20; 327.03)	243.23 (172.71; 305.86)	1,814.25 (1449.82; 2269.28)	510.86 (409.66; 612,71)
Medication	699.34 (541.90; 867.21)	1,262.61 (977.62; 1532.54)	525.19 (385.67; 652.49)	615.51 (463.68; 773.02)	761.87 (641.60; 857.07)
Inpatient treatment	175.36 (0.00; 355.48)	252.55 (0.00; 617.96)	591.00 (169.52; 1055.61)	636.96 (56.37; 1494.67)	411.76 (201.76; 648.71)
Median Direct medical costs	1,105.84 1,510.85 (1,178.57; 1,905.19)	1,344.21 2,023.85 (1,484.73; 2,583.72)	829.83 1,963.00 (1,341.32; 2,548.28)	3,501.15 4,663.04 (3,444.27; 6,015.10)	1,333.92 2,377.86 (1,995.54; 2,783.43)

Table III. *Univariate regression analysis. A* p-*value < 0.25 was considered significant*

Variables, values of cut-offs	Generalized linear model *p*-values	Logistic regression (≥€1,333.00) *p*-values
Demographics		
Sex, women	NS	NS
Age, continuous	NS	0.032
Education, high educational level	0.13	NS
Work force participation, employed	NS	0.020
Living with a partner	NS	NS
Interventional variables		
Treatment, day care	NS	NS
Disease-related variables		
Indication		
Osteoarthritis	Ref.	Ref.
Osteoporosis	0.1014	0.107
Back pain	0.1092	0.811
Fibromyalgia	<0.001	0.000
Comorbidities, continuous	<0.001	0.000
Quality of Life, continuous		
SF-36 – physical functioning	<0.001	0.004
SF-36 – role physical	<0.001	0.000
SF-36 – bodily pain	<0.001	0.001
SF-36 – general health	<0.001	0.000
SF-36 – vitality	<0.001	0.000
SF-36 – social functioning	<0.001	0.000
SF-36 – role emotional	<0.001	0.001
SF-36 – mental health	<0.001	0.000

physical. This indicates that optimal medical management of comorbidities is a cornerstone in reducing high direct medical costs in comprehensive rehabilitation programmes.

When comparing our results with the literature it is important to keep in mind that we considered 4 musculoskeletal conditions while published studies looked for predictors of costs regarding a single condition. Results of previous studies are therefore not directly comparable with ours. Indeed, medical condition was one of the strongest predictors of direct medical costs in this work. This result is consistent with a similar study targeting determinants of overall costs (direct medical and indirect costs) across 3 musculoskeletal conditions, which found the medical condition to be the single predictor of costs (30). In fact, only studies including several musculoskeletal disorders enable a direct and unbiased comparison of the economic burden of musculoskeletal diseases.

Predictors of direct costs identified in the present work are generally in line with available literature. We identified age as a statistically significant predictor of direct medical costs, which did not achieve significance in the final model addressing direct medical costs beyond the median. Indeed, age was identified as a significant predictor of direct medical costs in patients with RA (10), but this variable was dominated by patient-oriented outcomes measured by HRQoL instruments and other determinants in studies addressing direct medical costs beyond the median (9, 13). Associations between the scales of the SF-36 and direct medical costs are consistent with the available literature: poor scores in subscales of the SF-36 were significantly associated with the magnitude of direct costs incurred by OA patients (15) as well as with higher direct costs among RA patients (11). Considering that the SF-36 is measuring similar constructs as the HAQ, WOMAC and FIQ (4, 31), our results are in line with studies addressing a single musculoskeletal condition, which found patient-oriented outcomes, measured by disease-specific HRQoL instruments, to be a reliable predictor of direct costs (4–8, 10–14, 32).

The presence of comorbidity is an important predictor of costs among fibromyalgia patients (8, 12, 13). However, the impact of comorbidity on direct costs is still unclear among other musculoskeletal conditions. In a study including over 7,000 patients with RA comorbidity was, after the HAQ, the second strongest predictor of costs among clinical variables (10). In contrast, among RA and OA patients, comorbidity did not remain in the final model explaining costs (9, 11, 15). In 2 of these studies SF-36 scales were identified as strong predictors of direct costs (9, 15), which comes close to our

Table IV. *Regression models for prediction of direct medical costs. The table shows the final model of a generalized linear regression (GLM) with log link function and gamma distribution as well as a logistic regression model estimated with the same variables. In the logistic regression direct medical costs were dichotomized at the median of €1,333. The probability estimated with receiver-operating characteristics (ROC) curve that this logistic model can correctly distinguish between low and high cost was 76.4%*

	Linear outcome				Dichotomized outcome		
Variables in the final model	ß	$e^{ß}$*	SE	*p*-value	Odds ratio	95% CI	*p*-value
Age	0.0125	1.0125	0.0059	**0.034**	1.031	1.003–1.060	**0.030**
Indication							
Osteoarthritis	Ref.				Ref.		
Osteoporosis	0.7265	2.0678	0.1947	**<0.001**	1.412	0.590–3.377	0.439
Back pain	0.6247	1.8676	0.1783	**<0.001**	1.962	0.864–4.453	0.107
Fibromyalgia	1.2775	3.5876	0.2295	**<0.001**	6.208	2.060–18.709	**0.001**
Comorbidities	0.0288	1.0292	0.0229	0.207	1.157	1.033–1.296	**0.012**
SF-36 – role physical	–0.0074	0.9926	0.0022	**<0.001**	0.988	0.978–0.998	**0.014**
SF-36 – physical functioning	–0.0073	0.9927	0.0035	**0.036**	1.007	0.990–1.025	0.422
SF-36 – mental health	–0.0095	0.9905	0.0050	0.058	0.986	0.965–1.008	0.214
SF-36 – vitality	0.0137	1.0137	0.0050	**0.005**	1.013	0.990–1.037	0.266
SF-36 – social functioning	–0.0071	0.9929	0.0036	**0.047**	0.990	0.975–1.005	0.181

$e^{ß}$*: ratio of means, percentage increase in mean cost per unit increase in the covariate. Significant values are shown in bold.
CI: confidence interval; SF-36: Short-Form 36.

results. The SF-36 scales are powerful determinants of direct costs and might have dominated comorbidity in explaining the magnitude of costs in our work. Comorbidity was, in contrast, statistically a highly significant predictor of direct medical costs beyond the median in the present study. Since literature addressing the impact of comorbidity on direct medical costs beyond the median is scarce and contradictory, our results are hardly comparable. Among RA patients stratified by disease duration, comorbidity did not remain in the final model, while functional disability (HAQ) was the strongest variable associated with direct costs beyond the median (9). On the contrary, the presence of many comorbidity conditions was strongly associated with costs beyond the median among women with fibromyalgia (13).

Our results raise the question of what to target when designing cost-saving rehabilitation programmes. In order to reduce high direct medical costs in the long term, rehabilitation programmes need to focus rather on the societal perspective of functioning represented by the involvement in life situations like daily routine, instead of on the individual perspective of functioning represented by the execution of a task or action by an individual. In addition, adequate disease management programmes for patients with comorbidities need to be assured, since the presence of coexisting conditions were shown to exert a powerful influence on the incurrence of direct medical costs beyond the median. Finally, as the medical indication fibromyalgia was the outstanding determinant of direct medical costs beyond the median in our population, fibromyalgia should be targeted as a major public health issue. In summary, our findings stress the need for comprehensive rehabilitation programmes focusing on the reduction in participation restrictions and strongly taking into account the presence of comorbidities, if an impact on high direct medical costs is expected. Although we are not able to make inferences whether predictors of direct medical costs would also be determinants of indirect costs, we suppose that comprehensive and cost-saving rehabilitation programmes would not only lead to a decrease in direct medical costs, but also might translate into a decrease in indirect costs due to sick leave, for instance.

This work has some limitations. Firstly, we used a self-report retrospective standardized questionnaire to collect information on healthcare resources, and this kind of data source is susceptible to recall bias. Secondly, we extrapolated a part of the costs to obtain 1-year figures conservatively, assuming that resource use increases constantly. Thirdly, we decided to perform regression analysis only with complete data-sets. However, the bias introduced by inadequately imputing missing data was considered to be worse than the loss of power introduced by restricting the analysis to those observations with complete data. Fourthly, regarding the comparison between high and low costs it would also be meaningful to compare the first quarter of the distribution of direct medical costs, i.e. "very high costs" with the last quarter, i.e. "very low costs", but this was not possible due to our sample size. Fifthly, we have analysed data of patients undergoing rehabilitation, what restricts the generalizability of our results and might have influenced the appraisal of quality of life, since patients knew they would be treated in outpatient rehabilitation. Finally, it is also important to notice that the loss of power due to dichotomization of our dependent variable could be one reason the scales of the SF-36 physical functioning, social functioning and vitality did not remain in the final logistic regression model.

In conclusion, in our population almost the whole spectrum of functioning including body functions (SF-36 scale vitality) as well as activities and participation (SF-36 scales physical functioning, role physical and social functioning) in relation to the health condition (medical indication) and a personal factor (age) is needed to explain the distribution of direct medical costs. In predicting direct costs beyond the median, health condition (fibromyalgia, comorbidity) and an important participation component regarding how patients function in their daily activities as a result of physical health (SF-36 role physical), remained strong predictors.

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