

# Effect of subgroup-specific multimodal therapy on chronic spinal back pain and function—a prospective inpatient multicentre clinical trial in Germany

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## Abstract

Treatment modalities of spinal pain patients are discussed diversely, and different multimodal therapy programs have been developed. Purpose of the present study was to evaluate therapy outcome and effectiveness of an inpatient interdisciplinary and multimodal treatment program.

This prospective multicentre clinical trial has been performed with patients from orthopedic hospitals receiving a functional musculoskeletal therapy pathway. Outcome measures were pain intensity and back-specific function (Oswestry Disability Index) before (T1) and after the intervention (T2) as well as after 6 and 12 months (T3, T4). Statistical approach included parametric (*t* test) and nonparametric (Wilcoxon-test) tests and the calculation of effect sizes. Additionally, a statistical subgroup analysis based on selected parameters (degree of pain chronicity, gender, and age) was performed using linear mixed models.

In total, 249 patients (42.6% men, 57.4% women) with spinal pain were included, 133 patients were accessible for follow-up at T3 and 106 patients at T4.

Average pain (AP) reduced significantly ( $P < .001$ ) from T1 to T4 with an effect size of 0.99. Back-specific function also improved ( $P < .001$ ) over all measuring time points (TP) (effect size: 0.63). Furthermore, the statistical subgroup analysis demonstrated the efficacy of the treatment concept within the subgroup parameters chronicity degree and age.

A functional musculoskeletal therapy pathway including treatment of musculoskeletal dysfunctions appears to be beneficial in terms of treating pain and function. Pain chronicity and age seems to be factors influencing therapy outcome. Further studies are needed to examine the superiority of these inpatient programs for back pain including control groups.

**Abbreviations:** AP = average pain, CPI = v. Korff-characteristic pain intensity, MPSS = Mainz Pain Staging System, NRS = numeric rating scale, OPS = operations and procedure code, T1 = before the intervention/baseline, T2 = end of intervention, T3 = 6 months after the end of the intervention, T4 = 12 months after the end of the intervention, TP = measuring time points.

**Keywords:** chronic spinal pain, multimodal, musculoskeletal system, subgrouping, therapy pathways

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AS and JN contributed equally to this work.

The design of the study as well as data collection, data analysis, and data interpretation were developed from the cooperation partners (ANOVA [consortium of Non-Operative Orthopaedic Acute Hospitals] & Institute of Physiotherapy, Jena University Hospital) and were part of the cooperation agreement in the context of the research project. The University Hospital in Jena Institute of Physiotherapy got financial support for statistical analysis and data preparation. No funding was involved for the writing of the manuscript; none of the authors was a grant recipient. No other organizations were involved in funding.

All of the described examinations involving human subjects were conducted with the approval of the relevant ethics committee of the Jena University Hospital (ethics committee no. 3464–06/12).

There are no conflicts of interest.

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## 1. Introduction

Different mechanisms lead to the development of chronic spinal pain syndromes. Physical, psychological and psychosocial as well as behavioral features have been described contributing to the development of a chronic pain syndrome.<sup>[1]</sup> Classifications commonly differentiate between specific back pain described by distinct spinal pathology and non-specific back pain. Non-specific back pain is often considered as a homogenous group. Nevertheless, patients vary in their chronicity, pain intensity, functional level, and pain impact. However, they often get similar, but not targeted intervention, which inevitably affects the treatment success.<sup>[2]</sup> The need of identifying homogenous subgroups to optimize therapy interventions has already been claimed 20 years ago.<sup>[3]</sup> Since then various classification systems have been described.<sup>[4]</sup> Classification systems are based on biomechanical features as well as psychosocial or biopsychosocial characteristics.<sup>[1,2,5–8]</sup>

Furthermore, multimodal and multidisciplinary pain management programs have been established for chronic back pain. The majority of multimodal therapies are based on a cognitive-behavioral concept, targeting patients with non-specific back pain on the basis of psychosocial characteristics.<sup>[9,10]</sup> Nevertheless, various studies demonstrated complex musculoskeletal dysfunctions play a role in chronic back pain.<sup>[1,2,11–13]</sup> Without also addressing musculoskeletal dysfunctions in multimodal/multidisciplinary therapy concepts, the treatment of chronic back pain is likely to fail to gain sustained and efficient outcomes. Multimodal concepts should, therefore, integrate manual therapy approaches to provide individually targeted interventions to back pain patients. According to our knowledge to date, the majority of multimodal treatment strategies including manual therapy approaches have been of an outpatient character, predominantly combining manual therapy with specific exercise training and patient education.<sup>[14–21]</sup>

In Germany, a systematic inpatient treatment approach for patients with spinal pain syndromes has been established within the diagnosis-related group's system. In addition to the catalog of operations and procedure code (OPS) "multimodal pain therapy" (OPS 8–918), the OPS includes a procedure code "multimodal non-surgical complex treatment of the musculoskeletal system" (OPS 8–977). This procedure code was developed in cooperation with a consortium of Non-Operative Orthopaedic Acute Hospitals (ANOAH) to address complex diseases of the musculoskeletal system including back pain. The procedure code requires an inpatient multimodal interdisciplinary therapy program of at least 12 days with a specified diagnostic process and therapy approach.

As a consequence of the multimodal interdisciplinary diagnostic procedure, the patients are assigned to one of various treatment pathways targeting different therapy foci, for example, musculoskeletal function or psychological components.

The aim of this multicentre study was to investigate if a complex inpatient therapy program based on both a biopsychosocial and biomechanical musculoskeletal approach applying tailored intervention to chronic spinal pain patients is effective in decreasing pain and improving function. Furthermore, the sustainability of effects over a follow-up period of 12 months was of interest. The study concept was applied to a subgroup of patients treated with the OPS procedure 8–977, namely patients classified to participate in a functional musculoskeletal pathway.

Previously, the study concept was demonstrated in a pilot study, which showed a short-term therapeutic effect.<sup>[22]</sup> Regarding these results, a sample size estimation was performed and the current study design was developed.

## 2. Methods

### 2.1. Study design and participants

Based on the hypothesis that a tailored multimodal therapy program will lead to a sustainable reduction of pain and function, a prospective clinical multi-center study with 8 orthopedic hospitals was designed. Participants with chronic spinal pain syndromes were recruited from patients enrolled in the functional musculoskeletal therapy pathway after a specific multimodal interdisciplinary diagnostic procedure. The diagnostic process involved different procedures including an evaluation of psychosocial factors in order to ensure a comprehensive understanding of all influencing factors of the chronic musculoskeletal problem.

Part of the diagnostic procedures is an orthopedic-neurological physical examination in order to detect pathomorphological changes as well as a specific neuromuscular manual medicine examination to detect musculoskeletal dysfunctions. Evaluation of the musculoskeletal system is completed by an instrumental investigation of musculoskeletal function, for example, gait analysis or posturography. Additionally, a psychological evaluation and specific pain history taking (including questionnaires, e.g., Mainz Pain Staging System [MPSS], Von Korff Questionnaire for Grading the Severity of Chronic Pain) are part of the diagnostic process.

Inclusion and exclusion criteria are displayed in Table 1. Figure 1 displays the recruitment and experimental plan.

**Table 1**

### Inclusion and exclusion criteria.

#### Inclusion criteria

Age between 20 and 70 years	Spinal disorders/pain	With or without radiating pain
Presence of symptoms/disorders leastwise in two fields of the following 3 fields: Complex functional musculoskeletal findings, e.g.	Pathomorphological changes, e.g.	Psychosocial factors, e.g.
Functional chains and/or	Degenerative disorders spine	Cognitive-behavioral disorders
Motor-control impairments, coordination and/or postural dysfunctions	Discogenic spine disorders	Psychosocial risk factors
Vegetative dysfunctions	Spinal stenosis	

#### Exclusion criteria

Pain syndromes with imperative surgical indication	Radiculopathies with indication for surgical intervention
Systemic neurological diseases	Polyneuropathies
Rheumatic/inflammatory diseases	Pregnancy, lactation
Tumour diseases	Serious cardiopulmonary insufficiency (NYHA III and IV)
Pain syndromes due to non-orthopaedic diseases (e.g. from internal medicine)	Mental illness as main diagnosis, including F45.40 and F45.41
Mental disorders as a secondary diagnosis and psycho-social influences with primary or major impact on development and/or persistence of pain	Ongoing retirement application

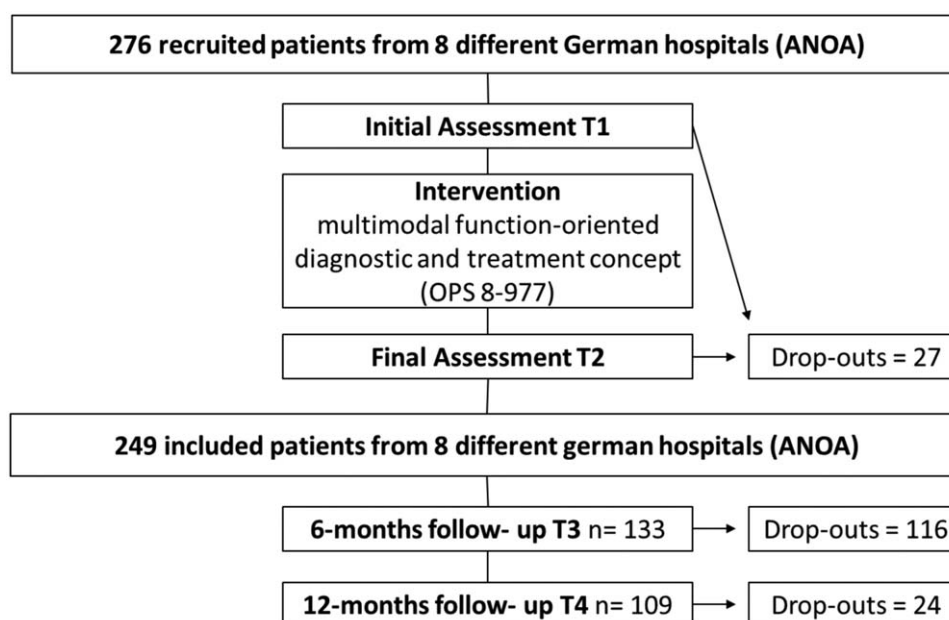


Figure 1. Participant flowchart.

## 2.2. Intervention

The functional musculoskeletal therapy pathway is part of an inpatient program of at least 12 days of treatment. It comprises at least 30 active or passive therapy units lasting 30 minutes on average. The obligatory program includes the following predefined therapy elements performed by different medical specialties. Medical treatment by specially trained physicians (or psychologists) contains at least 3 of the following 4 treatment methods:

- manual medicine
- reflex therapy (e.g., neural therapy, acupuncture)
- interventional pain medicine (infiltrations)
- psychotherapy.

Furthermore, physiotherapy by specialized therapists has to include at least 3 of the following 4 methods:

- manual therapy and neurophysiological based physiotherapy
- exercise therapy
- physical therapy
- relaxation techniques.

Allocation to therapy pathways, the composition of therapy elements and individual adaptations of therapy within the therapy process are carried out within interdisciplinary team meetings. This procedure ensured that every patient received a tailored individual therapy program based on individual needs concerning functional musculoskeletal, psychological, behavioral, and educational issues.

## 2.3. Outcome measures

Numerous parameters were collected within the entire study between 2014 and 2015. This article reports results of pain and back-specific function; results of additional psychological parameters will be reported elsewhere. Primary outcome criteria comprised differences in pain intensity obtained by the von Korff questionnaire for grading the severity of chronic pain.<sup>[23]</sup>

The secondary outcome criterion was back-specific function evaluated by the Oswestry Disability Index. Data were collected at the following time points (TP): before the intervention/baseline (T1), end of intervention, after 3 weeks (T2), 6 months after the end of the intervention (T3) and 12 months after the end of the intervention (T4).

## 2.4. Assessments

**2.4.1. Von Korff questionnaire for grading the severity of chronic pain—pain intensity.** The assessment for grading chronic pain by von Korff is a simple, short questionnaire assessing the severity of chronic pain disorders and the resulting impairment evaluating pain characteristics and its impact on person's activities. It has been evaluated concerning validity and reliability.<sup>[24]</sup> In this study, we used 2 items: average pain (AP) and v. Korff-characteristic pain intensity (CPI).

To assess the AP, the patients had to evaluate their AP intensity regarding the last 3 months with a numeric rating scale (NRS) of 0 "no pain" to 10 "worst pain".

The item CPI is calculated by the mean of numerical rating scale values for current pain, AP, and worst pain multiplied by 10 resulting in values between 0 and 100 points.

**2.4.2. Oswestry Low Back Pain Disability Index.** Back-specific function was detected with the Oswestry Low Back Pain Disability Index (ODI). This self-administered questionnaire consists of 10 items. Each item assesses an independent aspect of back pain and difficulties in different activities of daily life: pain intensity, personal care, lifting, walking, sitting, standing, sleeping, sex life, social life, and traveling. Items are scored from 0 (no disability) to 5 (highest disability). The score of this questionnaire displays a percentage of disability (1%–20% minimal disability, 21%–40% moderate disability, 41%–60% severe disability and 61%–80% crippled, 81%–100% bed-bound).<sup>[14,15,16]</sup> The assessment is valid, reliable and suitable for use in clinical practice.<sup>[25]</sup>

**Table 2****Characteristics of the participants due to age, chronicity degree and gender.**

Parameter	Participants (n=249)
Age (years, average value (SD), min/max)	53.4±10.6, 23 / 74
Chronicity degree (score MPSS, average value (SD))	2.3±0.6
Gender (male (in % of n) / female (in % of n))	106 (42.6%) / 143 (57.4%)

**2.4.3. MPSS.** The MPSS is an interview-administered assessment consisting of 10 items dividing pain syndromes in 3 degrees of chronicity (MPSS 1, MPSS 2, MPSS 3). MPSS 1 corresponds to the lowest stage and MPSS 3 to the highest stage of chronicity. The MPSS has been evaluated concerning validity.<sup>[26]</sup> This parameter has been added in the statistical analysis to characterize the statistical subgroup results in addition to age and gender.

**2.5. Statistical analysis**

Evaluation of the entire data was performed in the study center. Data were initially tested for normal distribution, followed by statistical analysis. Parametric *t* test for dependent samples was carried out if normal distribution of the sample was present. The nonparametric Wilcoxon test was used in absence of normal distribution. Furthermore, effect sizes according to Cohen (1992) were calculated and average values and effect sizes were visualized in charts.<sup>[27]</sup> Additionally, a statistical subgroup analysis was performed to analyze the impact of parameters such as the degree of pain chronicity (MPSS), gender, and age. Statistical subgroup analysis was performed using linear mixed models.

Ethics approval and consent of participants

All of the described examinations involving human subjects were conducted with the approval of the relevant ethics committee of the Jena University Hospital (ethics committee no. 3464-06/12), in accordance with national law and in accordance with the declaration of Helsinki of 1975 (in the current, revised version). Every enrolled patient agreed with the declaration of consent.

Furthermore, the study is registered retrospectively on the German clinical trials register ([www.drks.de](http://www.drks.de)) with the No. DRKS00011492.

**3. Results****3.1. Demographics**

In total, 276 patients with back pain syndromes were enrolled in this multicenter clinical trial completing an inpatient functional musculoskeletal therapy pathway. Of them, 249 participants (42.6% men, 57.4% women) with spinal pain syndromes (55.4% lumbar spine, thoracic spine 4%, cervical spine 34.5%, radiating pain to the lower extremities 2%, radiating pain to the upper extremities 2.8%, 1.2% missing value), provided complete data sets at T2 and were eligible for inclusion in data analysis. With consideration of pain localisation, 26.5% of the patients had single-regional, 21.7% double-regional and 50.6% multi-regional pain localisations (1.2% missing values). Table 2 displays the demographic data of patients; drop-out numbers are shown in Figure 1. Reasons for exclusion were: missing values in the questionnaires, missing questionnaires, missing MPSS, lack of consent form, exclusion criteria fulfilled, ongoing retirement application, and non-return of documents. Of the 249 included patients, 133 were accessible for follow-up at T3 and 106 patients were included as well at T4.

**3.2. Total group analysis**

Total group analysis refers to the outcomes of all 249 study participants concerning pain intensity and back-specific function. Analysis of AP showed significant differences ( $P < .001$ ) for the entire group at all TP compared to baseline. Perceived AP was 6.02 (SD +/- 1.79) at baseline and declined steadily over all TP: T2 4.73 (SD +/- 1.86), T3 4.28 (SD +/- 2.24), and T4 4.19 (SD +/- 2.00). In order to assess the clinical relevance, effect size calculation according to Cohen (1992) was performed.<sup>[27]</sup> The effect size was 0.99 (T1 vs T4), meaning a large effect (Table 3).

CPI was significantly decreased ( $P < .001$ ) from 65.42 (SD +/- 15.97) (T1) to 46.99 points (SD +/- 16.02) (T4). Again, CPI steadily declined over all TP: T2 49.93 (SD +/- 23.05), and T3 47.32 (SD +/- 20.53). The effect size was 1.05 (T1 vs T4), indicating a large effect size again (Table 3).

Back-specific function significantly improved over all TP ( $P < .001$ ). ODI showed a moderate disability at baseline with 36.37% (SD +/- 14.50), which steadily declined over all TP to 27.24% (SD +/- 14.76) at T4. The grade of disability did not change, in spite of the improvement. The effect size was at 0.63 (by comparison T1 vs T4), which means a medium effect (Table 3).

**Table 3****Results of the measured parameters due to total group analysis.**

		Outcome parameter		Outcome <i>t</i> test		
		Mean	SD ±	Comparison	<i>P</i>	Effect size Cohen <i>d</i>
Average pain (AP) (0–10, 10 = maximum AP)	T1	6.02	1.79			
	T2	4.73	1.86	T1-T2	<.001	0.71
	T3	4.28	2.24	T1-T3	<.001	0.89
	T4	4.19	2.00	T1-T4	<.001	0.99
v. Korff - characteristic pain intensity (CPI) (0–100, 100 = maximum CPI)	T1	65.42	15.97			
	T2	49.93	16.02	T1-T2	<.001	0.97
	T3	47.32	23.05	T1-T3	<.001	0.97
	T4	46.99	20.53	T1-T4	<.001	1.05
Oswestry Disability Index (ODI) (0–100%, 100% = maximum disability)	T1	36.37%	14.50%			
	T2	26.19%	14.20%	T1-T2	<.001	0.71
	T3	27.92%	16.33%	T1-T3	<.001	0.56
	T4	27.24%	14.76%	T1-T4	<.001	0.63

**Table 4**  
**Results due to interactions concerning the statistical subgroup analysis; interactions by time points (TP), chronicity (Mainz Pain Stage System, MPSS), age and gender and its consequences for average pain (AP) and characteristic pain intensity by von Korff (CPI).**

	P AP	P CPI
TP	.00	.00
MPSS	.00	.00
MPSS * TP	.85	.73
Gender	.09	.09
Gender * TP	.50	.73
Age	.00	.00
Age * TP	.02	.00

AP= average pain, MPSS= Mainz Pain Stage System, CPI=characteristic pain intensity by von Korff, TP=time points.

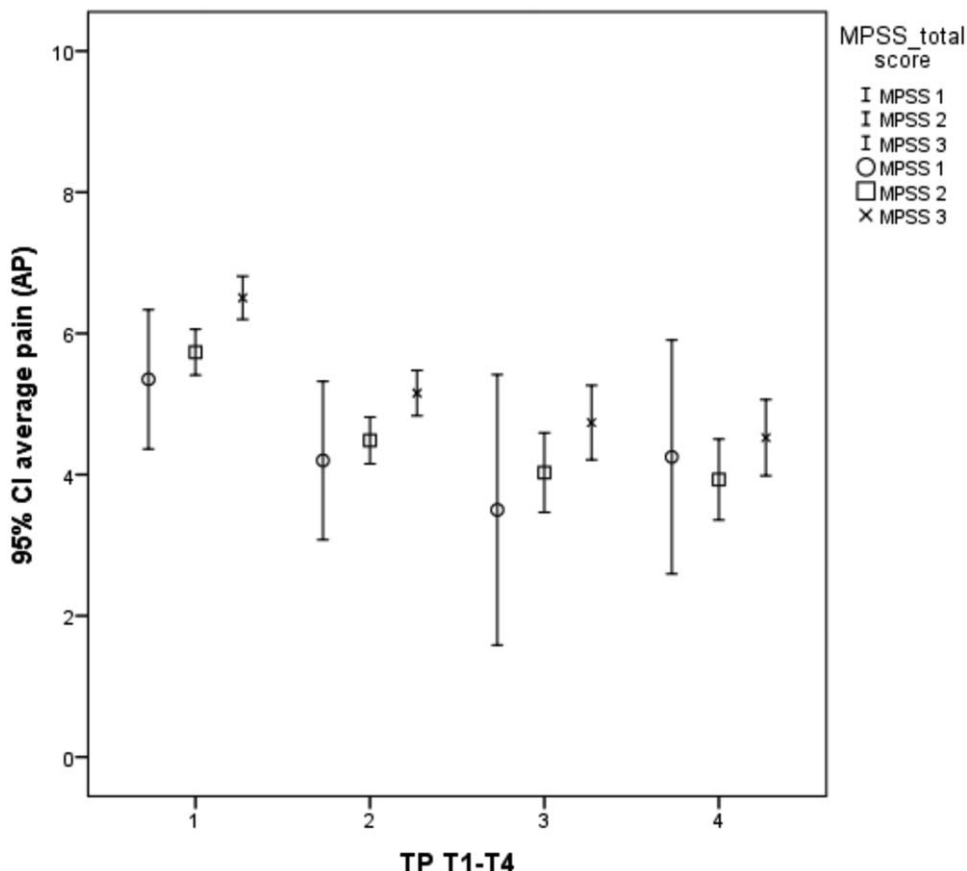
**3.3. Subgroup analysis**

According to the degree of pain chronicity, significant differences in the parameters AP and CPI were detected (Table 4). Figure 2 and Figure 3 show that the participants with the highest degree of pain chronicity (MPSS 3) indicated higher pain in comparison to participants with lower degrees of pain chronicity. According to AP, patients with MPSS 3 improved from 6,5 (SD +/- 1,79; T1) to 4,52 (SD +/- 1,77; T4) whereas patients with MPSS 2 resp. MPSS 1 reported reduced pain from

5,73 (SD +/- 182; T1) resp. 5,35 (SD +/- 2,11; T1) to 3,93 (SD +/- 2,15; T4) resp. 4,25 (SD +/- 1,98; T4). Same issue is given if the CPI is considered. Patients, assessed as MPSS 3, changed from 70,03 (SD +/- 13,19; T1) to 49,92 (SD +/- 18,68; T4). In contrast to all patients assessed as MPSS 2 resp. 1. Here the appropriate means improved from 62,36 (SD +/- 16,86; T1) resp. 60,67 (SD +/- 18,05; T1) to 44,37 (SD +/- 22,04; T4) resp. 49,59 (SD +/- 18,81; T4). However, all participants presented decreased pain intensities (AP & CPI) regardless of their grade of chronicity (MPSS) and therefore benefited from the treatment.

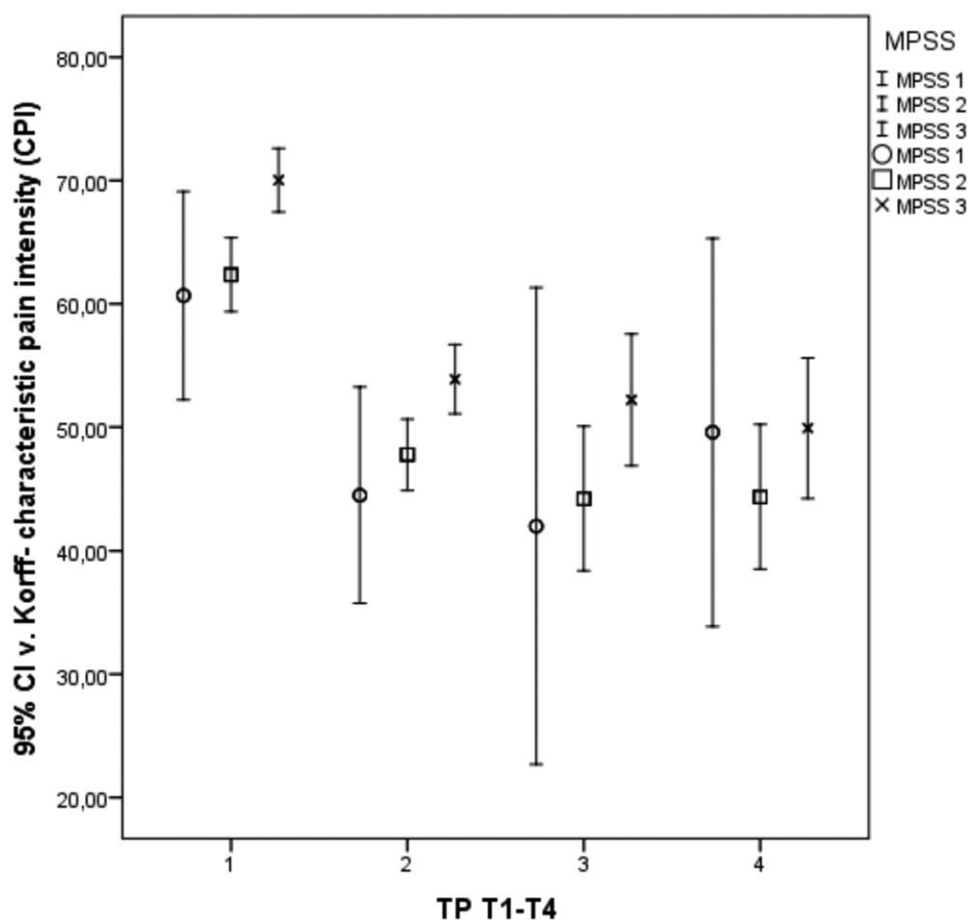
Furthermore, statistical analysis showed significant differences concerning age (Table 4). Comparing participants under and above 55 years demonstrated differences of pain intensities in time response (Fig. 4 and Fig. 5). Older participants reported pain intensities stagnating or even slightly increasing after the intervention for AP (T3: 4,66 +/- 2,23; T4: 4,85 +/- 1,66) and for CPI (T3: 51,09 +/- 22,61; T4: 54,12 +/- 16,28). In younger participants, pain intensities reduced further for AP (T3: 3,85 +/- 2,20; T4: 3,52 +/- 2,10) and for CPI (T3: 43,05 +/- 22,97; T4: 39,73 +/- 21,96). Obviously, age has an impact on the intervention outcome and younger participants benefit over a longer period than older participants.

Subgroup analysis for gender revealed that neither significant differences between women and men in general nor significant time-related differences were present (Table 4). Accordingly, gender did not affect the outcome of the intervention at all.



**Figure 2.** The development of AP due to the subgroup analysis of the degrees of pain chronicity (MPSS) by time between TP1 to TP4. Reported AP is always higher in patients with MPSS 3 in comparison to patients with a lower state of pain chronicity. AP=average pain, MPSS=Mainz Pain Stage System.





**Figure 3.** The development of CPI due to the subgroup analysis of the degrees of pain chronicity (MPSS) by time between TP1 to TP4. Reported CPI is almost throughout higher in patients with MPSS 3 in comparison to patients with a lower state of pain chronicity. CPI=characteristic pain intensity by von Korff, MPSS= Mainz Pain Stage System.

#### 4. Discussion

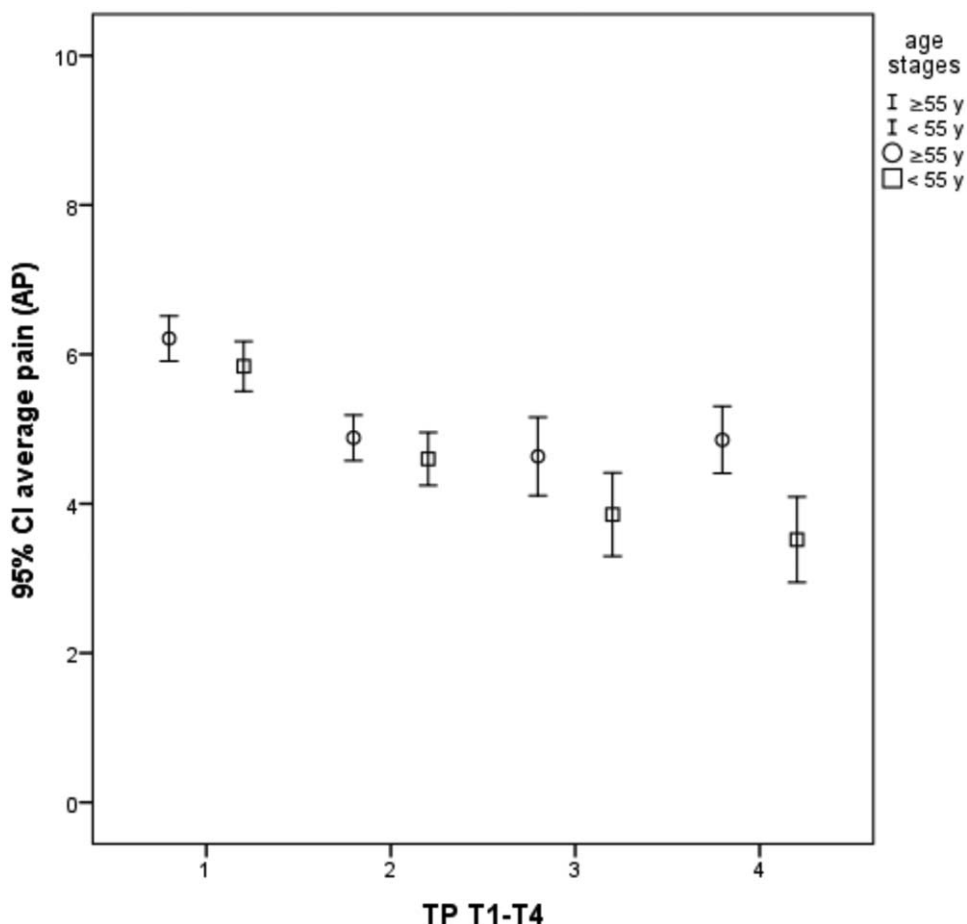
In this prospective multicentre study, we evaluated short-, intermediate, and long-term effects of a multimodal interdisciplinary inpatient treatment program targeting a functional musculoskeletal therapy pathway. Results showed a significant reduction of pain intensities and back-specific functional ability at discharge of the hospital treatment as well as at 6 and 12 months. The largest effects in both observed domains were detected immediately after the intervention. Nevertheless, further reduction of outcome values was present until 12 months (T4) after the intervention.

Subgroup analysis regarding age detected the long-term reduction of pain intensities primarily in younger participants. In elderly patients, a reduction of pain intensities was not maintained over the entire observation period of 12 months; however, it was over 6 months. A possible explanation for this effect might be the assumption that degenerative changes of the spine are less frequently for younger patients. Hence they respond better to a functional musculoskeletal therapy approach. Nevertheless, all participants (regardless of age, gender or pain chronicity) stated less pain after the intervention up to 12 months. Furthermore, a higher degree of chronicity (MPSS 3) resulted in higher pain levels. Gender had no effect on outcome parameters.

Effect sizes regarding pain intensities (AP, CPI) achieved values between 0.99 and 1.05, meaning a large effect. Concerning back-specific function, the effect size was at 0.63 (medium effect).

Considering the effect size, it has to be mentioned that calculated values only represent the statistical magnitude of the effect without taking clinical aspects into account.<sup>[28]</sup> Evaluating the clinical relevance in addition to the calculated effect sizes referring to Cohen,<sup>[27]</sup> results of comparable investigations should be included. With regard to pain intensity, Farrar et al<sup>[29]</sup> evaluated pain with the visual analog scale (VAS) considered a difference of at least 2 points respectively 30% at least in a scale of “0 to 10” as clinically relevant. Regarding AP, our presented data just narrowly fall below this required target (difference of 1.83 points). Concerning CPI, Farrar et al indicated a difference of 20 to be of clinical relevance. Again, this value was nearly reached with a score of 18.43. Nevertheless, we regarded the results concerning pain intensity as clinically relevant, as pain reduction of about 30% occurred in both cases (AP: 30.4%; CPI: 28.2%). Furthermore, pain reduction is even higher in the subgroup of participants younger than 55 years. Considering back-specific function, the minimal clinically relevant difference is regarded between 4 and 10.5 points (between 8 and 21%),<sup>[25]</sup> which positively corresponds to our values with an improvement of 9.13% (4.6 points). Therefore, the results of back-specific function are of clinical relevance.

The literature shows various inpatient multimodal interdisciplinary therapy programs of different treatment strategies. Meng et al<sup>[30]</sup> evaluated a standardized back school program as part of a multimodal multidisciplinary 3-week inpatient rehabilitation



**Figure 4.** The development of AP due to the subgroup analysis of age by time between TP1 to TP4. Reported AP is always higher in patients above 55 years in comparison to younger patients. AP=average pain.

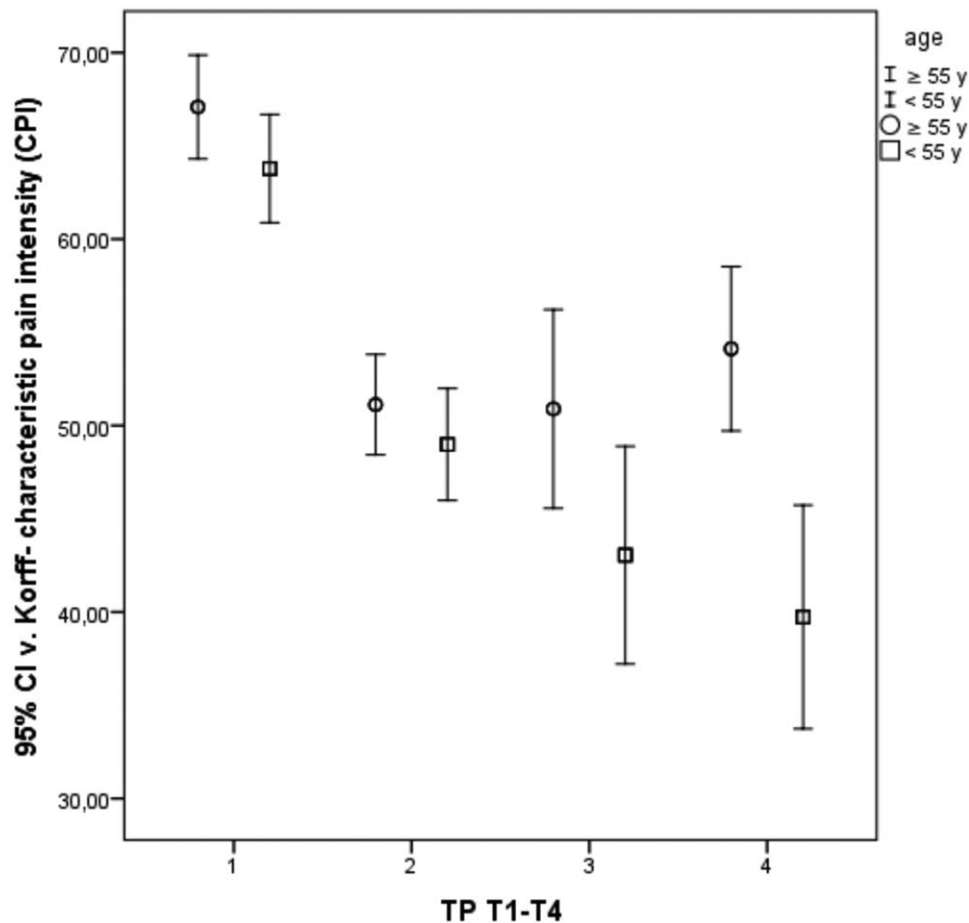
clinic of German statutory pension funds focussing on illness knowledge, behavioral and health outcomes. Furthermore, the influence of work-related interventions on functional capacity,<sup>[31]</sup> the difference between function-centered rehabilitation versus pain-centered rehabilitation<sup>[32,33]</sup> or auxiliary cognitive behavioural treatment within inpatient rehabilitation programs<sup>[34,35]</sup> has been investigated. Most of these multimodal programs did not include the evaluation of pain intensities. Only Kool et al<sup>[33]</sup> collected pain changes with an NRS between 2 different rehabilitation groups (function-centered treatment vs pain-centered treatment). Solely the function-centered treatment group achieved a small postinterventional decrease of pain (NRS -0.25; SD +/- 2.1), which changed into an increase of pain (NRS +0.35; SD +/- 2.1) 3 month after the intervention. The pain-centered treatment group reported an increase of pain immediately (NRS +0.55; SD +/- 1.9) and 3-month after the intervention (NRS +0.89; SD +/-1.9). Overall, the effect size for pain was small (0.42). In comparison with these findings by Kool<sup>[33]</sup> our data show a higher decrease of pain intensity (VAS -1.83 for AP) and a large effect size (0.99). In order to valuate these results one has to take into account that the rehabilitation program of Kool et al had a duration of 3 weeks containing 70 therapy hours for the function-centered treatment group whereas our therapy pathway within a hospital setting lasted on average 12 days with 30 therapy units á 30 minutes.

Nevertheless, all of these previous investigations have been performed within the setting of a rehabilitation center and not an

orthopedic hospital. To our knowledge, there are no other investigations of a multimodal therapy program within an orthopedic hospital setting. Again it has to be acknowledged that the here presented therapy program is obviously shorter than a typical multimodal rehabilitation program lasting on average 3 weeks with up to 100 hours of therapy units.

Moreover, a tailored musculoskeletal approach including manual therapy was not the center of focus in these studies. At present, to the best of our knowledge, published complex therapy programs including manual therapy have been solely performed in outpatient settings.<sup>[14-21]</sup> All of these studies combined manual therapy with specific exercises and in 2 studies patient education in addition. The majority of studies showed a significant reduction of pain and disability<sup>[14-17,20]</sup> in the intervention group including manual therapy. Despite this, treatment programs of these outpatient studies are not of a comparable complexity as the hereby evaluated functional musculoskeletal therapy pathway. We believe that the implementation of manual therapy and the individually tailored musculoskeletal approach in a multimodal inpatient setting including pain therapy, exercise therapy, physical therapy, and patient education might be an essential cause explaining the distinct reduction in pain and disability demonstrated by our data.

Nevertheless, there is further evidence needed demonstrating the superiority of inpatient programs in back pain. Härkäpää et al<sup>[36]</sup> demonstrated a higher decrease in a pain index, a higher



**Figure 5.** The development of CPI due to the subgroup analysis of age by time between TP1 to TP4. Reported CPI is always higher in patients above 55 years in comparison to younger patients. CPI=characteristic pain intensity by von Korff.

frequency of back exercises and a higher self-estimation of treatment benefits of an inpatient versus outpatient rehabilitation program.

#### 4.1. Limitations

A limitation concerning this study is the lack of a control group. Designing a study concept including a control group was considered but failed as finding an appropriate control group appeared not possible. Comparing this complex multimodal therapy program with non-multimodal stationary therapy programs was not eligible as these last on average 5 to 7 days and are not comparable in terms of therapy intensity. Therefore, positive clinical effects may have been biased by an overall training effect or even a placebo effect triggered by the human care or behavioral medical aspects. However, further studies have to overcome this problem and should include control groups.

Secondly, the high drop-out rate of 47% after 6-month and in total 56% after 1 year has to be discussed as another study limitation. Patients were contacted by sending a postal questionnaire. A part of the drop-outs was caused by changed mailing addresses, other patients failed to send the questionnaires back. As telephone contacting was originally not intended, reasons for drop-out<sup>[37]</sup> were impossible to determine. Nevertheless, analyses of pain and disability (AP, CPI, and ODI) at T2 between patients with complete data and lost follow-ups showed

no significant differences concerning these outcome parameters. Therefore, there is no indication that drop-outs might have differed essentially at T3 and T4 in terms of therapy outcome. Despite this, comparable drop-out rates concerning postal questionnaires were found in a literature analysis with 52.45%<sup>[37]</sup> and 54%<sup>[38]</sup> and as well in one of the discussed rehabilitation studies.<sup>[31]</sup> We cannot rule out that the high drop-out rate might have biased the results. Therefore, further studies should try to control drop-out rates by including telephone reminders and collect detailed data concerning drop-out reasons.

Additionally, there are discussions about subgroup analysis in the back pain field for different reasons, for example their lack of statistical power.<sup>[39,40]</sup> Furthermore, additional factors for targeting treatments (e.g. genetics, psychological, activity-related behavioral approaches) have been identified. Therefore, the results of the subgroup analysis identifying pain chronicity and age as important factors influencing therapy outcome as well as additional factors have to be further assessed in future investigations.

Continuative studies will have to demonstrate the specificity of the treatment in this indication-related subgroup of patients. Appropriate investigations should ideally be randomized, controlled, and investigator-blind studies. Notwithstanding, these preconditions are commonly difficult to employ in investigations concerning clinical therapy modalities.

To our knowledge, this is the first study within the setting of orthopedic hospitals investigating a multimodal interdisciplinary



treatment pathway tailored to the individual needs of patients including manual and reflex therapy, physical therapy, interventional pain therapy, and biopsychosocial elements. The study showed that the examined diagnostic and treatment approach in patients with complex musculoskeletal dysfunction results in a sustained, significant and clinically relevant modification of pain perception and back-specific function. Moreover, study results suggest that the evaluated therapy program is suitable for patients with a high degree of chronicity suffering from predominantly multi-regional back pain syndromes and is not limited just to low back or neck pain.

Overall, a functional musculoskeletal therapy pathway including indication-specific subgrouping and the implementation of musculoskeletal dysfunctions in a multimodal diagnosis and treatment process appears to be useful and promising. Further studies including control groups are needed to support these findings.

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