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Bibliographic Data	
Authors	Ris I, Søgaard K,Gram B, and et al.
Title	Does a combination of physical training, specific exercises and pain education improve health-related quality of life in patients with chronic neck pain? A randomized control trial with a 4-month follow up
PMID	27598552
Citation	Manual Therapy 26 (2016) 132-140
Other information if relevant	The trial was registered on www.ClinicalTrials.gov NCT01431261 and at the Regional Scientific Ethics Committee of Southern Denmark S-20100069.

Methods	
Aim of study	To compare the difference in clinical effectiveness of a multimodal exercise intervention consisting of physical training, specific exercises, and pain education with pain education alone on physical HR-QoL (health related quality of life) in patients with chronic neck pain.
Design	Assessor single-blind randomized controlled superiority multicenter clinical trial

Participants	
Population from which participants are drawn	Participants were recruited in Denmark via the participating clinics/centers by their treating physiotherapist or at their first contact with the clinic. The study involved both primary and secondary health care.
Setting (location and type of facility)	The interventions were performed at the site of patient recruitment, mostly physiotherapy clinics in Denmark.
Age	adults 18 years of age, minimum, mean age 45.1 years
Sex	51 men, 149 women, total 200 at baseline
Total number of participants for whom outcome data were reported	At the primary endpoint of 4 months, 200 participants were analyzed using intention-to-treat analyses. The number tested at follow-up was 89 (88%) in the exercise group, and 75 (76%) in the control group. Outcome data were reported on 125 participants in the per protocol analyses.
Inclusion criteria	1. Minimum aged 18 years 2. Minimum of 6 months of neck pain 3. Reduced neck function (Neck Disability Index > 10) 4. Completed diagnostic procedures (e.g. medical investigations) 5. Neck region as the primary pain area
Exclusion criteria	1. Clinically confirmed radiculopathies 2. Progressive medical treatment 3. Unstable social/working conditions 4. Pregnancy 5. Known current fractures 6. Beck Depression Inventory-II score > 29 7. Conditions limiting participation

Other information if relevant	There were no significant differences between groups in participants' baseline sociodemographic, clinical characteristics, or outcome measure scores, except that the control group had more females (80.1%) compared to the exercise group (68.3%). Mean duration of symptoms for participants was 9 years.

Intervention Groups

Group 1	
Group name	Exercise group (combined pain education, specific exercises and graded physical activity training)
Number in group	101 at baseline
Description of intervention	Participants received 4 sessions (1½ hours each, once per month) of pain management education focusing on understanding/ acceptance of pain, goal setting, and participation in social- and work-related contexts based on a cognitive concept. They also received 8 sessions of 30 minute instruction in exercises and physical training. The progressive exercises were individually tailored with a focus on: 1) neck flexor and extensor function, 2) standing balance, oculomotor training, and neuromuscular function of the shoulder girdle. The graded physical activity was a self-chosen physical activity program, such as walking or cycling, with the starting level of training duration set to 20% below the patient's indication of capability, increasing the time factor every second week by 20%. Patients were instructed to perform the exercises twice daily and physical training 3 times a week for 4 months.
Duration of treatment period	4 months
Co-interventions if reported	none
Additional information if relevant	

Group 2	
Group name	Control Group
Number in group	99 at baseline
Description of intervention	Participants received 4 sessions (1½ hours each, once per month) of pain management education focusing on understanding/ acceptance of pain, goal setting, and participation in social- and work-related contexts based on a cognitive concept. (Same as exercise group).
Duration of treatment period	4 months
Co-interventions if reported	none
Additional information if relevant	

Primary outcome	
Outcome name and criteria for definition	The primary outcome was the change in Physical Component Summary Score (of the Short Form Health Survey (SF36-PCS) measured 4 months after baseline. The minimal clinically important difference (MCID) for a change score is 3 to 5 points.
Time points measured and/or reported	At baseline and 4 months after baseline by a blinded assessor.
Differences between groups	ITT-analyses showed a statistically significant difference in the change score of the SF36-PCS between groups at the 4 month follow-up in favor of the exercise group: -1.83 SF36-PCS points (95% CI: -3.86 to -0.21) P value = 0.03. The exercise group improved significantly by 2.75 points (95% CI: 1.23 to 3.55) on the SF36-PCS from baseline to the 4 month follow-up while the control group only improved 0.92 points (95% CI: -0.48 to 1.84), a non-significant change. These improvements did not quite meet the MCID of 3 to 5 points, but the confidence intervals of the exercise group included the MCID showing a small clinically worthwhile effect.
Additional information if relevant	One adverse event of increased pain due to exercise was registered in the exercise group. The control group had a significantly higher dropout rate compared with the exercise group (24% vs. 12%).

Secondary outcomes	
Outcome name and criteria for definition	The secondary outcome measures were: 1. SF36-MCS = Short Form 36 Mental Component Summary; 2. EQ-5D =EuroQol-5 dimensions; 3. EQ-VAS = EuroQol Visual Analogue Scale; 4. NDI = Neck Disability Index; 5. BDI-II = Beck Depression Inventory-II; 6. PB = Pain Bothersomeness; 7. PSFS = Patient-Specific Functioning Scale; 8. TSK = Tampa Scale of Kinesiophobia; 9. GPE = Global Perceived Effect. 10. Several clinical tests
Time points measured	At baseline and 4 months after baseline by a blinded assessor.
Differences between groups	Secondary outcomes revealed statistically significant improvement for the exercise group for SF36-MCS and BDI-II. 1. Results showed a statistically significant difference in the change score of the SF36-MCS between groups at the 4 month follow-up in favor of the exercise group: -2.26 SF36-MCS points (95% CI: -4.41 to -0.12) P value = 0.01. The exercise group improved significantly by 2.45 points (95% CI: 1.05 to 3.85) on the SF36-MCS from baseline to the 4 month follow-up while the control group only improved 0.19 points (95% CI:-1.46 to 1.84), a non-significant change. These improvements did not quite meet the MCID of 3 to 5 points, but the confidence intervals of the exercise group included the MCID showing a clinically worthwhile effect. 2. Results showed a statistically significant difference in the change score of the BDI-II between groups at the 4 month follow-up in favor of the exercise group: -2.65 points (95% CI: -4.33 to -0.95) P value = 0.01. The exercise group improved significantly by 2.43 points (95% CI: 1.33 to 3.53) on the BDI-II from baseline to the 4 month follow-up while the control group worsened by -0.22 points (95% CI:-1.53 to 1.10), a non-significant change.

Additional information if relevant	ITT analysis results were reported. Adherence to the treatment intervention was 'good' for 68 patients (67%) in the exercise group, and 60 patients (61%) in the control group.
Conclusions	
Key Conclusions Of Study Authors	- Chronic neck pain patients receiving pain education, exercises and graded physical training significantly improved their physical HR-QoL compared with the controls receiving pain education alone. This multimodal intervention may be an effective intervention for chronic neck pain patients. - Significant improvements in the exercise group were also demonstrated in mental HR-QoL and in mood (BDI-II) compared with the control group. - Per protocol analyses which included only participants with good adherence to the intervention (attended 75% of education and/or exercise/training sessions) strengthened the results from the ITT-analyses. The per protocol analyses revealed a significantly increased effect of the exercise intervention on SF36-PCS increasing from 2.75 to 3.39, accentuating the importance of good compliance with the interventions. Future studies should examine barriers to compliance with exercise and training. - The exercise group increased their psychological well-being significantly more compared with the control group. The per protocol analyses strengthened the results from the ITT-analyses revealing a significantly increased effect with good compliance of the exercise intervention on the mental HR-QoL and in mood (BDI-II) accentuating the importance of good compliance with the interventions. This indicates that improvements are related to compliance, and confirms the positive effect/influence of physical training on psychological outcomes. - The improvement in physical HR-QoL was significantly better in the exercise group by 1.83 points. Although the MCID for SF36-PCS is 5 points for chronic neck pain patients undergoing cervical fusion, it has been shown to be as low as 2 points under less risky circumstances which may be more relevant to exercise. From this perspective, the current changes for the exercise group actually reached the MCID (2.75 in the exercise vs 0.92 in the control group). Future studies should define the relevant MCID of SF36-PCS in this group.

Risk of bias assessment		
Domain	Risk of bias Low High Unclear	Comments
Random sequence generation *(selection bias)*	Low	A computer-generated randomization schedule, stratified by clinic and onset (traumatic/non-traumatic) was created using SAS statistical software with 1:1 allocation, using random block sizes of 2, 4, and 6.
Allocation concealment *(selection bias)*	Low	The allocation sequence was concealed from the assessor in sequentially numbered, opaque, sealed and stapled envelopes. The handling of the envelopes was performed by other persons than the investigators.
Blinding of participants and personnel *(performance bias)*	High	Because of the nature of the interventions, it was not possible to blind participants or physiotherapists.The lack of blinding does not prejudice the conclusions.
Blinding of outcome assessment *(detection bias)*	Low	All outcome measures were obtained by an investigator who was unaware of group allocation. The allocation sequence was concealed from the assessor. The statistician was blinded to group allocation during the initial statistical analyses. All authors were masked to group allocation as well for analysis and interpretation of results.
Incomplete outcome data *(attrition bias)*	High	Loss to follow up (no longer interested) was significantly higher in the control group (24%) compared with the exercise group (12%). All participants lost to follow-up were included in the ITT analysis.
Selective outcome reporting? *(reporting bias)*	Low	The trial was registered with www.ClinicalTrials.gov NCT01431261 and at the Regional Scientific Ethics Committee of Southern Denmark S-20100069.
Other bias		Intention to treat analysis was used.

Sponsorship if reported		
Study funding sources if reported	The Research Fund of the Region of Southern Denmark, Danish Rheumatism Association, Research Foundation of the Danish Association of Physiotherapy, Fund for Physiotherapy in Private Practice, and Danish Society of Polio and Accident Victims funded the study.	
Possible conflicts of interest for study authors	None declared	
Notes:		

Comments by DOWC staff

- The findings of this study showed that a 4-month intervention for chronic neck pain patients containing pain education, specific exercises and graded activity training showed a significant effect, although clinically small, on improved HR-QoL, as well as on psychological factors, compared with controls receiving pain education alone. Good adherence increased the effect in favor of the exercise group.
- A multimodal pain education/exercise/ physical training intervention is more effective in improving physical and mental quality of life, and mood than a pain education intervention alone for patients with chronic neck pain.
- The improvement in physical HR-QoL was significantly better in the exercise group by 1.83 points compared to the control group, and the improvement from baseline to the 4 month follow-up was 2.75 points in the exercise group. The MCID on the physical SF36-PCS is 3 to 5 points, so the improvements in the exercise group did not quite reach the MCID, but since the confidence intervals of the exercise group included the MCID, it is possible that a small, clinically worthwhile effect may be present.
- The change of SF36-PCS in the exercise group did not show increased physical fitness. This may be due to performing too little exercise and physical training below recommendations.
- The participants in the exercise group had an additional eight visits to the physiotherapist compared with the control group, resulting in a potential risk of attention bias. These non-specific effects of added attention in the exercise group could have influenced the results in favor of the exercise group.
- The control group had a significantly higher dropout rate compared with the exercise group (24% vs. 12%). This may be an indication that participants in the control group were not satisfied with their intervention of pain education alone or did not find it worthwhile or effective for their chronic neck pain.
- Study strengths included a large sample size with adequate statistical power to detect clinically meaningful effects, trial registration, a pre-specified protocol, a defined primary outcome, design features known to minimize bias such as assessor blinding, concealed allocation, an intention-to-treat and per protocol analysis, multicenter involvement, including both primary and secondary health care, support for generalizability of the results, strong external validity, and a priori consensus in interpretation of blinded results.
- The main limitations of the study were lack of blinding of therapists and patients, the high number of treating physiotherapists (35) that may have confounded treatment fidelity, unequal matching of the interventions in format and time, numerous secondary outcomes, and a high drop-out rate in the control group of 24%.

Assessment by DOWC staff	
Overall assessment as suitability of evidence for the guideline ☐ High quality ☒ Adequate ☐ Inadequate	This adequate quality study provides some evidence that a 4-month intervention for chronic neck pain patients containing pain education, specific exercises and graded activity training shows a significant effect, although clinically small, on improved physical and mental health related quality of life compared with controls receiving pain education alone. Good adherence increased the effect in favor of the exercise group.
If inadequate, main reasons for recommending that the article not be cited as evidence	

Additional references if relevant
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