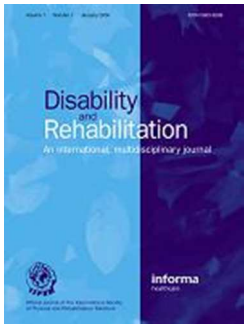


Does Manual Therapy Provide Additional Benefit To Breathing Retraining In The Management Of Dysfunctional Breathing? A Randomised Controlled Trial

Journal:	*Disability and Rehabilitation*
Manuscript ID:	TIDS-09-2013-034.R1
Manuscript Type:	Research Paper
Keywords:	Dysfunctional Breathing, Breathing retraining, Manual therapy, Physiotherapy

Implications for Rehabilitation

Dysfunctional breathing (DB) is associated with significant patient morbidity but often goes unrecognised, leading to prolonged investigation and significant use of health care resources. There is mounting, but not conclusive evidence supporting the use of breathing retraining for the management of this condition. However, increased knowledge is required about the epidemiology, aetiology, pathophysiology and natural history of this disorder. A large scale RCT evaluating the efficacy of breathing retraining in primary DB is warranted.

Physiotherapists are using manual therapy (MT) as an adjunctive treatment for patients with DB. However, there is little consensus regarding the nature of the proposed connective and muscular tissue lesions that these techniques purport to address. In addition, there is no validated tool to identify and quantify these abnormalities and their potential response to therapy. Therefore, the additional use of MT provides no further benefit and cannot be recommended in the clinical management of this condition

Does Manual Therapy Provide Additional Benefit To Breathing Retraining In The Management Of Dysfunctional Breathing? A Randomised Controlled Trial

M Jones[a], F Troup[b], J Nugus[c], M Roughton[d], ME Hodson[c,e], C Rayner[f], F Bowen[g], JA Pryor[c]

INTRODUCTION

Dysfunctional breathing (DB) is a psychologically (primary) or physiologically (secondary) based respiratory disorder associated with significant patient morbidity [1]. It is characterised by an abnormal breathing pattern [2-5], presented by combinations of erratic breathing [2, 6, 7], episodic breath holding and sighing [2, 8] or hyperventilation [2, 8]. In DB, thoracic excursion predominantly occurs from the upper rather than lower chest and diaphragm [8]. DB occurs in approximately 6-11% of the general patient population and accounts for symptoms in up to 40% of patients' in general medical outpatient clinics [2]. Rapid recognition of DB is essential to increase the chance of appropriate management [6].

Although the precise mechanisms underlying DB are poorly understood, the focus of treatment is reversal of over-breathing through respiratory physiotherapy [1]. Current physiotherapy management consists of breathing retraining, with the patient being taught diaphragmatic breathing control, relaxation techniques and DB education [1, 9, 10]. Treatment aims to restore and maintain a normal diaphragmatic breathing pattern and in some cases, re-programme the respiratory center to trigger inspiration at a higher level of carbon dioxide [1, 10]. Evidence exists to support this approach in both primary DB [11-14] and DB occurring secondary to chronic cardiorespiratory disease, such as asthma [6, 15] and cardiac failure [16,17].

Increasingly, physiotherapists in the UK [10] and internationally [18] are using manual therapy (MT) as a treatment component in the management of primary and secondary DB [19]. Proponents of these techniques suggest that DB produces structural and functional changes to

the musculoskeletal system [20]. In particular, dominance of the accessory muscles of respiration, thoracic spine hypo-mobility, increased tonicity of the abdominal muscles restricting diaphragmatic movement, costovertebral dysfunction or increased myofascial tone are seen in these patients. Additionally, due to the Bohr effect [21], the lowered levels of carbon dioxide inhibit the transfer of oxygen from haemoglobin to the tissue cells, which may lead to ischemia, fatigue and pain [10] and the evolution of myofascial trigger points [20]. Such trigger points purportedly change the activation of the entire kinetic chain [22], altering both movement and breathing patterns, impeding normal respiratory function secondary to poor posture. These musculoskeletal adaptations are believed to influence respiratory function, perpetuating the abnormal respiratory pattern [10]. As such, proponents argue that patients with DB may find normalisation of their breathing pattern difficult with breathing retraining alone, and advocate MT ('muscle energy techniques' 'diaphragm doming' and 'rib raising') to reverse the musculoskeletal abnormalities [10].

Although benefits of MT in DB are reported anecdotally, no robust evidence exists to validate these claims. This study sought to investigate the hypothesis that MT produces additional benefit when compared with breathing retraining alone in a group of patients with primary DB.

METHODS

Subjects

Between July 2007 and January 2009, 60 subjects aged 18-88 years were recruited to this parallel study from the respiratory outpatient clinic at a London postgraduate teaching hospital and three private physiotherapy practices. Each patient had a clinical diagnosis of DB following a positive Nijmegen score [4, 23] (score >23). Patients with metastatic disease, osteoporotic disease, respiratory infection or DB as a consequence of asthma or cardiac disease were excluded from the study.

Following written consent, computerised randomisation was undertaken by an independent researcher, with subjects assigned to either respiratory management (standard treatment group; n=30) or respiratory management plus MT (intervention group; n=30). The study protocol was approved by Brompton, Harefield & NHLI Ethics Committee.

Interventions

Following randomisation, throughout the study, subjects were individually assessed and treated at each session, according to the study protocol, by one of two experienced physiotherapists. Data collection took place at Royal Brompton & Harefield NHS Foundation Trust. Both groups received standardised respiratory physiotherapy management: 1) an explanation and education of the mechanisms and symptoms associated with DB, including developing self-awareness of breathing pattern; 2) identification of "trigger factors" to DB response, plus management / minimisation strategies 3) breathing retraining involving diaphragmatic breathing control at rest in sitting, lying or standing [1, 10] with gradual normalisation of respiratory frequency; 4) diaphragmatic breathing during and following exertion; 5) a diaphragmatic breathing regimen to practice at home for 4 x 10 minutes daily at an agreed respiratory frequency; 6) a breathing retraining programme compact disc [24] with pre-recorded tracks providing auditory cues for accurate practice of breathing control techniques. This programme was reaffirmed at each visit, and progression made based on individual subject response. In addition, subjects randomised to the intervention group received an individualised selection of MT techniques (based on the limited existing literature in this area), in response to musculoskeletal abnormalities identified following a standardised assessment. This involved observation of dynamic and static posture, assessment of active and passive ranges of movement (neck, thoracic, shoulder joints), muscle length tests (cervico-scapulo-thoracic musculature), joint accessory glides (costovertebral, cervical, thoracic, glenohumeral, acromioclavicular joints), myofascial palpation and rib expansion measurement. Techniques employed included 1) muscle and joint mobilisation

techniques, for example Maitland mobilisations [25], muscle energy techniques, trigger point therapy, myofascial and positional release techniques [26]; 2) diaphragm doming [27]; 3) rib raising [28].

Outcome measures

The primary outcome measure was change from baseline in the Nijmegen score. The Nijmegen Questionnaire has been validated as a tool for the diagnosis of DB [4]. A score of >23 has been shown to correlate positively with DB [23]. Secondary outcome measures were change from baseline in 1) spirometry measured by forced expiratory volume in one second (FEV_1), forced vital capacity (FVC); 2) breath hold time [3] (a short breath hold time is usually associated with a low or unstable resting P_aCO_2; 3) exercise capacity (6-minute walk test [29] with oximetry, undertaken in accordance with American Thoracic Society Statement Guidelines [30]; 4) Hospital Anxiety and Depression Scale (HADS) [31]; 5) musculoskeletal measurements: cervical lateral flexion (a gross measure of tightness in neck muscles), bilateral shoulder flexion with spine in neutral (a measure of restriction in upper back) and chest expansion, through circumferential measurement of rib expansion at the level of the 7^{th} thoracic vertebra.

Subjects were assessed on entering the study, with outcome measures undertaken at baseline, then repeated at 2, 4, 8, 12 and 26 weeks, before a treatment session based on their allocated group. The outcome measures were undertaken by an independent observer blinded to the subject's treatment allocation. In addition to planned outcome measurement sessions, subjects in both groups received further physiotherapy treatment dependent on individual clinical assessment findings, as reflective of contemporary clinical practice.

Sample size calculation

Using existing data from the Lung Function Laboratory, at Royal Brompton & Harefield NHS Foundation Trust, the predicted mean baseline Nijmegen score was 27 (SD 10). It was calculated that 25 subjects were required in each group to provide a study with 80% power to show an absolute reduction in Nijmegen score of 9 and 17 in the standard and intervention group respectively at a significance level of 0.05. To allow for a 20% dropout during the course of the study 60 subjects were recruited (30 in each arm).

Statistical analysis

Continuous data are summarised as mean (SD) and categorical data as N (%). The effect of MT on all outcome measures was assessed using a mixed-effects linear regression model. The data from each subject visit were entered into the model, with subjects declared as a random effect due to the repeated nature of the data. The estimate of the treatment effects were adjusted for time and baseline values, and presented as mean difference between the groups along with 95% confidence intervals. Paired t-tests were used to assess the within group changes from baseline to the final visit for each subject. A secondary analysis comparing the change in each group from baseline to final visit was carried out using un-paired t-tests. Missing data from subjects who withdrew from the study was not imputed. All analyses were performed using Stata 10 (StataCorp, Texas) and a p value of less than 0.05 was used to determine statistical significance. All other p values are presented for completeness only.

RESULTS

60 subjects (30 per group) were recruited into the trial. The analysis comprised all 57 subjects who achieved at least 1 follow up visit, (3 subjects; 1 respiratory group, 2 MT group, failed to attend any further sessions following baseline assessment). Twenty-seven and 28 subjects in the respiratory and MT arm respectively, completed baseline and a minimum of 3 follow-up

sessions. In addition, to the 5 pre-determined outcome measurement sessions, some subjects from both study groups received additional interim treatment sessions as reflective of clinical practice. Subjects in the MT group received more treatment sessions than those in the standard therapy group (Respiratory Group 6.3 (SD 2.2) sessions vs. MT Group 9.1 (SD 3.4) sessions; $p<0.001$). Data were analysed on an intention to treat basis, with no cross-over between study groups. All treatments were delivered in full without any documented adverse events. The respiratory group had higher Nijmegen scores at baseline, and was younger (Table 1). At baseline, demonstrable musculoskeletal (MSK) problems, consistent with those described in the literature, were identified in all subjects in both groups. Subjects had one or more of the following MSK problems, presented in different combinations and to differing degrees in individual subjects: over active accessory muscles, postural abnormalities, reduced range of movement affecting cervical and thoracic spine, glenohumeral joint with poor scapulohumeral rhythm, myofascial trigger points and tight paracervical and thoracic musculature. The identification of techniques for each individual subject was based on assessment findings undertaken before each treatment session. Most commonly used techniques included: mobility exercises, postural education, muscle and joint mobilisation techniques (Maitland mobilisations and rib rising), trigger point therapy / myofascial and positional release techniques, muscle energy techniques and diaphragm doming.

Insert table 1 here

There was no significant difference between the intervention and standard treatment groups for the primary outcome (Nijmegen score), or any secondary outcomes (Table 2). After adjusting for baseline values, the Nijmegen score of the MT group fell by an average of 2.8 points less than the respiratory group (95% CI (-1.1, 6.6) $p=0.162$) (Table 2); For Nijmegen score, lower values are associated with less severe symptoms. Additionally, there was no difference in the rate of

change for Nijmegen score between the two groups (Figure 1). There was no treatment effect on lung function, with both FEV_1 (p=0.453) and FVC (p=0.914) showing little evidence of effect.

Inset table 2 here

Insert figure 1 here

Within group comparisons showed significant improvements in the primary and several secondary outcomes for both study groups (Table 3). In the MT group the Nijmegen score fell by 12.6 (9.0) points and by 17.6 (13.6) points in the respiratory group (p<0.001 for both), with normalisation of Nijmegen seen in over 65% of subjects (21/28, MT group and 19/29, respiratory group; p=0.56). Statistically significant improvements were also seen in both groups for HADs, breath hold length, bilateral shoulder flexion and cervical flexion.

Insert table 3 here

DISCUSSION

In this study, statistically significant improvements in DB, as documented by decreased Nijmegen score and normalisation of the Nijmegen score in over 65% of subjects in both study groups. In addition, within group improvements were also found in several secondary outcomes including HADS, 6-minute walk, breath hold test and some musculoskeletal measurements. However, contrary to our hypothesis, the application of MT techniques demonstrated no additional benefit to breathing retraining.

Although this study was not specifically designed to investigate the efficacy of breathing retraining *per se*, the improvement in Nijmegen score and the number of subjects with a

normalised Nijmegen score seen in both groups is consistent with the existing, but limited literature in this area. A pilot study [12] evaluating four different approaches to the management of primary DB reported significant improvements in symptoms following a 12-week course of breathing retraining and relaxation. This finding was supported by a controlled study [13], which established a 10-week programme of breathing exercises using an incrementally adjusted ventilatory retraining device, was successful in the management of primary DB. Significant improvements in psychological factors, symptom complaints and respiratory dimensions were also noted. In an uncontrolled interventional trial [14], Han et al concluded that breathing retraining with a physiotherapist over 2-3 months, resulted in significantly reduced Nijmegen score and anxiety levels in 92 subjects with primary DB; positive results were attributed to reduced respiratory frequency observed following treatment. DeGuire et al reported breathing retraining through paced diaphragmatic breathing had both short term [16] and lasting effects [17] on respiratory physiology and highly correlated with a reduction in reported functional cardiac symptoms in 41 patients with cardiac disease and associated DB. The results of our study concur with an earlier RCT [6]; evaluating physiotherapy based breathing retraining versus nurse-led asthma education for asthmatic patients with DB. This group reported half their subjects showed a fall in Nijmegen score, which correlated with a clinically relevant improvement in quality of life following physiotherapy; this improvement was maintained in a quarter of subjects' 6-months later. These findings were supported by a 2007 RCT [15], which concluded that breathing retraining and relaxation (The Papworth Method) significantly reduced respiratory symptoms and DB, while improving health related quality of life and adverse mood, compared with usual care in a group of 36 patients with asthma. In this study, based on literature of other chronic respiratory disease, a clinically significant improvement in HADS [32] was found in both study groups, and the 6-minute walk test [33] in the respiratory management group. Furthermore, statistically significant improvements were observed in secondary musculoskeletal indices in both study groups; this suggests that these changes may have

occurred secondary to reversal of DB and normalisation of Nijmegen through breathing retraining.

We believe this is the first RCT to evaluate the use of MT in the management of primary DB. Osteopathic and chiropractic MT dates back to the beginning of the 20th century and focuses on mobilising the ribs and thoracic spine to increase thoracic expansion, with claims of improved lung function, quality of life, arterial oxygen content and lymphatic return [20, 21]. The use of such techniques for non-spinal or extremity pain has caused controversy and debate in the literature [19]. Although the proposed physiological mechanisms underpinning these techniques remain poorly understood, reports of improved outcomes following their application exist for asthma [34, 35], pneumonia [36] and paediatric respiratory infections [37]. Bronfort et al (2001) [34] undertook a prospective clinical case series combined with an observer-blinded, pilot randomised clinical trial investigating the effect of chiropractic spinal manipulative therapy (SMT) in addition to optimal medical management in 36 paediatric subjects with mild and moderate asthma. They concluded that after 3 months of combining chiropractic SMT with optimal medical management, subjects rated their quality of life substantially higher and their asthma severity substantially lower, with improvements maintained at 1-year follow up. However, the authors stated that the results could not be attributed to the specific effects of chiropractic SMT alone. Furthermore, no control group data were published for comparison.

A recent RCT [35] investigating the effects of osteopathic manipulative treatment (OMT) on paediatric patients with asthma reports a statistical but clinically insignificant improvement in peak expiratory flow rate (PEFR) following intervention. However, they report within group not between group comparative data. In addition, there was no evidence of statistical adjustment for baseline inequalities, with the control group demonstrating more severe airflow obstruction. In a well-designed RCT, Balon et al (1998) [38] investigated the effects of chiropractic SMT versus

simulated chiropractic SMT over 4-months in paediatric subjects with asthma. They reported no significant difference in outcome for PEFR at 2 or 4-months, symptoms of asthma, use of ß-agonists, quality of life, spirometric measurements or airway responsiveness. They concluded that chiropractic SMT provided no additional benefit to usual medical care in children with mild or moderate asthma. Indeed, this paper accounts for more than 50% of the subjects (1 of 3 papers) considered in a recent Cochrane systematic review [19], which concluded "there is insufficient evidence to support the use of manual therapies for patients with asthma". This finding was confirmed by a recent UK evidence report which reviewed chiropractic and osteopathic MT [39].

Limitations of the study

This study was conducted in a single center; however subjects with DB were recruited from both primary and secondary care. The recruited subjects were predominantly female (43:17), but this is consistent with the existing literature.

In this study sham MT was not employed and all clinical interventions were undertaken by two experienced, but un-blinded physiotherapists. However, computer aided randomisation occurred centrally and all baseline and subsequent assessments were undertaken by an independent single physiotherapist who had no knowledge of subjects study arm allocation.

Although data collection was incomplete for some subjects (3 subjects lost to follow-up), 27 and 28 subjects in the respiratory and MT arm respectively, completed baseline and a minimum of 3 follow-up sessions, within the range of our original power calculation (minimal n=25 in each study arm). Indeed, although not statistically significant, the improvements in Nijmegen score, our primary outcome, were greatest in the control (respiratory) group – making it unlikely that a true benefit for MT was missed.

We recognise that our decision to apply multiple and individualised MT may make it difficult to tease out the therapeutic benefit of different individual and / or combinations of techniques. However, a pragmatic choice was made to use a relevant but restricted number of MT, which mirrors contemporary clinical practice, where a range of MT is often applied together. Therefore, this study cannot advise regarding additional techniques not employed, nor can possible interactions between the techniques be excluded.

Implications

DB is associated with significant patient morbidity but often goes unrecognised, leading to prolonged investigation and significant use of health care resources. There is mounting, but not conclusive evidence supporting the use of breathing retraining for the management of this condition. However, increased knowledge is required about the epidemiology, aetiology, pathophysiology and natural history of this disorder. A large scale RCT evaluating the efficacy of breathing retraining in primary DB is warranted.

With reference to MT, there is little consensus regarding the nature of the proposed connective and muscular tissue lesions, that these techniques purport to address. In addition, there is no validated tool to identify and quantify these abnormalities and their potential response to therapy. Therefore, before any further application of such techniques in patients with DB is justifiable, further research centered on these issues is required.

Conclusion

Breathing retraining is currently the mainstay of treatment for patients with DB. Based on the results of this study, the additional use of MT provides no further benefit and cannot be recommended in the clinical management of this condition.

(Words 3012)

Trial Registration

Full protocol available at http://clinicaltrials.gov/ct2/show/NCT00895219

Registration number NCT 00895219

Ethical Approval: The study protocol was approved by Brompton, Harefield & NHLI Ethics Committee.

Funding: The Sir Siegmund Warburg Voluntary Settlement

Acknowledgements

The authors would like to thank the patients who participated in the study, Juliana Burgess who undertook the computer randomisation and the Sir Siegmund Warburg Voluntary Settlement for its financial support, without which the study would not have been undertaken. We also wish to thank Dr Robert Wilson, Clinical Director Respiratory Medicine, Royal Brompton & Harefield NHS Foundation Trust, for his support of the project from its inception, and Dr Andy Jones for his help with preparation of the manuscript.

Declaration of interest statement: The authors report no declaration of interest

REFERENCES

[1] Bott J, Blumenthal S, Buxton M, et al. on behalf of the British Thoracic Society Physiotherapy Guideline Development Group. Guidelines for the physiotherapy management of the adult, medical, spontaneously breathing patient. Thorax 2009;64(Suppl I):i1–i51.

[2] Morgan MDL. Dysfunctional breathing in asthma: is it common, identifiable and correctable? Thorax 2002;57(Suppl II):ii31-ii35.

[3] Gardner WN. The pathophysiology of hyperventilation. Chest 1996;109:516-534.

[4] van Dixhoorn J, Duivenvoorden HJ. Efficacy of Nijmegen questionnaire in recognition of the hyperventilation syndrome. J Psychosom Res 1985;29:199–206.

[5] Folgering H. The pathophysiology of hyperventilation disorder. Monaldi Arch Chest Dis 1999;54:365–71.

[6] Thomas M, McKinley RK, Foy C, et al. Breathing retraining for dysfunctional breathing in asthma: a randomised controlled trial. Thorax 2003; 58:110-115

[7] Han JN, Stegen K, Simkens K, et al. Unsteadiness of breathing in patients with hyperventilation syndrome and anxiety disorders. Eur Respir J 1997;10:167–76.

[8] Hormbrey J, Jacobi MS, Patil CP, et al. CO2 response and pattern of breathing in patients with symptomatic hyperventilation compared with asthmatic and normal subjects. Eur Respir J 1988;1:846–52.

[9] Cluff RA. Chronic hyperventilation and its treatment by physiotherapy: discussion paper. Journal Royal Society Medicine. 1984 October; 77(10): 855–862.

[10] Innocenti DM, Troup F. Hyperventilation. In: Pryor JA, Prasad SA, eds. Physiotherapy for Respiratory and Cardiac Problems. 4th edition. Edinburgh: Churchill Livingstone, 2008:529-549

[11] Lum LC. Physiological considerations in the treatment of hyperventilation syndromes. J Drug Res 1983;8:1867–72.

[12] Kraft AR, Hoogduin CA. The hyperventilation syndrome. A pilot study on the effectiveness of treatment. Br J Psychiatry 1984;145:538–42.

[13] Grossman P, De Swart JC, Defares PB. A controlled study of a breathing therapy for treatment of hyperventilation syndrome. J Psychosom Res 1985;29:49–58.

[14] Han JN, Stegen K, De Valck C, et al. Influence of breathing therapy on complaints, anxiety and breathing pattern in patients with hyperventilation syndrome and anxiety disorders. J Psychosom Res 1996;41:481–93.

[15] Holloway EA and West RJ. Integrated breathing and relaxation training (the Papworth method) for adults with asthma in primary care: a randomised controlled trial. Thorax 2007;0:15

[16] DeGuire S, Gevirtz R, Kawahara Y, et al. Hyperventilation syndrome and the assessment of treatment for functional cardiac symptoms. Am J Cardiol 1992;70:673–7.

[17] DeGuire S, Gevirtz R, Hawkinson D, et al. Breathing retraining: a three-year follow-up study of treatment for hyperventilation syndrome and associated functional cardiac symptoms. Biofeedback Self Regul 1996;21:191–8.

[18] Bradley D and Clifton-Smith T. Breathing works for asthma. Kyle Cathie: 2003

[19] Hondras MA, Linde K, Jones AP. Manual therapy for asthma. Cochrane Database Syst Rev. 2002;(4):CD001002.

[20] Chaitow L, Bradley D, Gilbert C. Multidisciplinary Approaches to Breathing Pattern Disorders Edinburgh: Churchill Livingstone, 2002

[21] Magarian GJ. Hyperventilation syndromes: infrequently recognised common expressions of anxiety and stress. Medicine 1982;61(4):219-236

[22] Lucas K et al Latent Myofascial Trigger Points: Their Effects on Muscle Activation and Movement Efficiency. Journal of Bodywork and Movement Therapies 2004;8(3):160-166

[23] Vansteenkiste J, Rochette M, Demedts M. Diagnostic tests of hyperventilation syndrome. European Respiratory Journal 1991;4:393-399

[24] Pitman A. Hyperventilation Syndrome - A breathing retraining programme. Audio compact disc:2005 Available from http://www.physiohypervent.org/index.php?m=0&i=7

[25] Maitland G Vertebral Manipulation 7th edition Edinburgh: Elsevier, 2005

[26] Ward R (ed) Foundations for osteopathic medicine. Baltimore: Williams and Wilkins, 1997

[27] Wallace E, McPartland J, Jones J, et al. In: Ward R (ed) Foundations for osteopathic medicine. Williams and Wilkins, Baltimore 1997

[28] Rowane W, Rowane M 1999 An osteopathic approach to asthma. Journal of the American Osteopathic Association 99(5): 259-264

[29] Camarri B, Eastwood PR, Cecins NM, et al. Six minute walk distance in healthy subjects aged 55 - 75 years. Respiratory Medicine 2005;100(4) 658-665

[30] Nici L, Donner C, Wouters E, Zuwallack R, Ambrosino N, Bourbeau J, et al American on behalf of the ATS/ERS Pulmonary Rehabilitation Writing Committee Thoracic Society/European Respiratory Society Statement on Pulmonary Rehabilitation. Am J Respir Crit Care Med Vol 173. pp 1390–1413, 2006

[31] Zigmoid AS, Snaith RP. The Hospital Anxiety and Depression Scale. Acta Psychiatrica Scandinavica 1983;67(6):361–37

[32] Puhan MA, Frey M, Büchi S, Holger J, Schünemann J. The minimal important difference of the hospital anxiety and depression scale in patients with chronic obstructive pulmonary disease. Health and Quality of Life Outcomes. 2008; 6:46

[33] Wise RA and Brown CD. Minimal Clinically Important Differences in the Six-Minute Walk Test and the Incremental Shuttle Walking Test Journal of Chronic Obstructive Pulmonary Disease.2005; (2):125–129

[34] Bronfort G, Evans RL, Kubic P, et al. Chronic pediatric asthma and chiropractic spinal manipulation: A prospective clinical series and randomized clinical pilot study. Journal of Manipulative and Physiological Therapeutics 2001;24(6):369–77.

[35] Guiney PA, Chou R, Vianna A, et al. Effects of Osteopathic Manipulative Treatment on Pediatric Patients With Asthma: A Randomized Controlled Trial. Journal of the American Osteopathic Association 2005;105:7-12

[36] Noll D, Shores J, Bryman P, et al. Adjunctive osteopathic manipulative treatment in the elderly hospitalized with pneumonia. Journal of the American Osteopathic Association 1999; 3:143-152

[37] Kline C Osteopathic manipulative therapy, antibiotics and supportive therapy in respiratory infections in children. Journal of the American Osteopathic Association 1965;65:278-281

[38] Balon J, Aker PD, Crowther ER, et al. A comparison of active and simulated chiropractic manipulation as adjunctive treatment for childhood asthma. N Engl J Med. 1998;Oct 8;339(15):1013-20.

[39] Bronfort G, Haas M, Evans R, et al. Effectiveness of manual therapies: the UK evidence report. Chiropr Osteopat. 2010; Feb 25;18:3.

Measurement	Respiratory group N=30	Manual Therapy group N=30	p value
Age (years)	41.7 (13.5)	50.8 (13.0)	0.001*
Male	10 (33.3)	7 (23.3)	0.390
Weight (kg)	78.1 (24.4)	70.8 (16.0)	0.183
Height (m)	170.6 (10.5)	166.5 (8.2)	0.096
BMI	26.7 (7.5)	25.4 (6.0)	0.476
Nijmegen score	38.6 (9.5)	31.5 (6.9)	0.001*
HAD Anxiety	11.6 (4.2)	10.0 (4.5)	0.174
HAD Depression	6.5 (3.0)	5.9 (3.9)	0.534
Breath hold (seconds)	25.5 (13.7)	22.8 (9.1)	0.367
Cervical flexion right (cm)	36.8 (9.3)	35.4 (7.9)	0.542
Cervical flexion left (cm)	33.5 (8.1)	33.3 (7.3)	0.953
Bilateral shoulder flexion (degrees)	152.1 (29.3)	145.6 (31.6)	0.411
Chest expansion (cm)	3.57 (1.76)	3.98 (1.44)	0.329
FEV_1	2.97 (0.69)	2.66 (0.81)	0.207
FVC	3.65 (1.27)	3.42 (0.99)	0.437
S_PO_2 pre walk test (%)	96.7 (1.31)	97.0 (1.1)	0.423
HR pre walk test (bpm)	76.5 (15.7)	73.4 (9.2)	0.423
Borg Dyspnoea pre walk test	1.86 (1.25)	2.09 (1.36)	0.509
Borg Fatigue pre walk test	2.11 (2.14)	1.91 (2.03)	0.726
6MWT distance (m)	523.3 (139.5)	465.3 (144.6)	0.123
Borg Dyspnoea post walk test	3.91 (1.75)	3.89 (1.86)	0.966
Borg Fatigue post walk test	3.46 (2.28)	3.27 (2.81)	0.775

Table 1: Characteristics and baseline values of study subjects *All values mean (SD) except male, which is N (%). * Indicates statically significant difference*

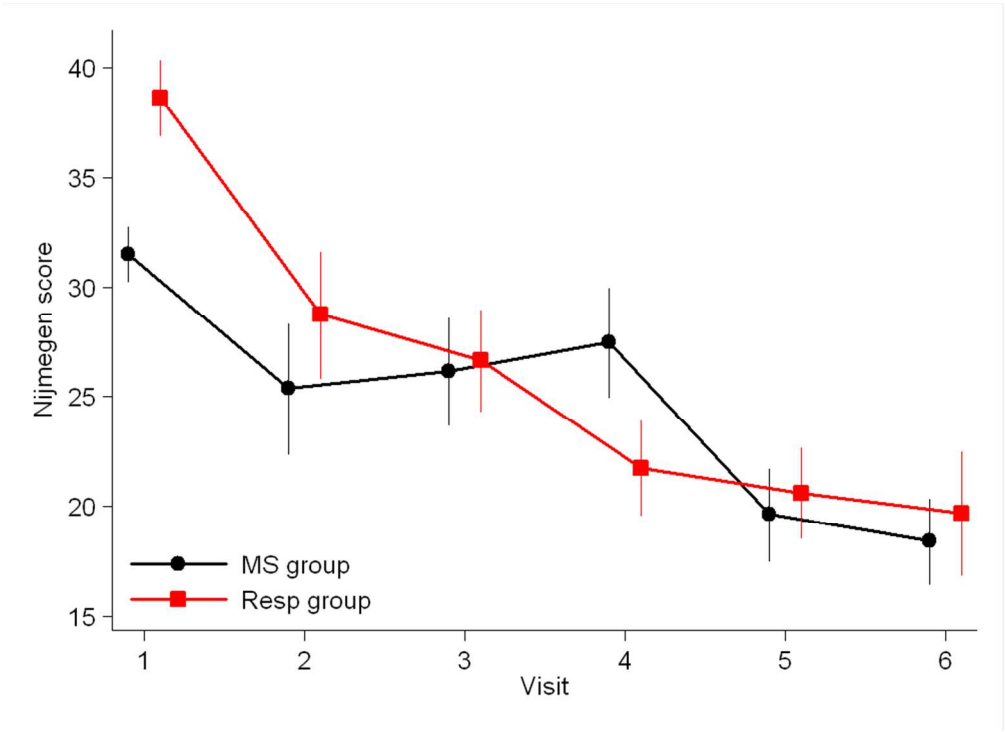
Measurement	Treatment effect	95% CI		p value
Nijmegen score	2.8	-1.1	6.6	0.162
HAD Anxiety	0.6	-0.8	2.0	0.394
HAD Depression	0.3	-0.6	1.2	0.505
Breath hold (seconds)	1.4	-2.0	4.8	0.412
Cervical flexion right (cm)	-1.8	-4.4	0.9	0.190
Cervical flexion left (cm)	-0.7	-2.8	1.4	0.518
Bilateral shoulder flexion (degrees)	4.1	-2.3	10.5	0.213
Chest expansion (cm)	-0.1	-0.4	0.2	0.632
FEV_1	0.02	-0.04	0.09	0.453
FVC	0.01	-0.09	0.10	0.914
S_PO_2 pre walk test (%)	0.0	-0.3	0.3	0.824
HR pre walk test (bpm)	1.2	-1.2	3.6	0.326
Borg Dyspnoea pre walk test	0.0	-0.5	0.4	0.960
Borg Fatigue pre walk test	0.1	-0.4	0.7	0.651
6MWT distance (m)	-10.5	-32.9	11.8	0.356
Borg Dyspnoea post walk test	-0.1	-0.5	0.4	0.789
Borg Fatigue post walk test	-0.1	-0.6	0.5	0.733

Table 2: Analysis of primary and secondary outcomes *All results adjusted for baseline and visit number. The treatment effect represents the difference between the changes in the manual therapy (MT) relative to the respiratory arm for each variable. A positive treatment effect indicates that the final value for that parameter was greater in the MT arm relative to that in the respiratory arm. For Nijmegen score it should be noted that a lower score is desirable, therefore, a positive treatment effect for this variable means patients in the MT group decreased by less than those in the respiratory group.*

Measurement	Change from baseline to last visit			
	MT group	p value	Resp group	p value
Nijmegen score	-12.6 (9.0)	<0.001*	-17.6 (13.6)	<0.001*
HAD Anxiety	-2.5 (3.8)	0.002*	-4.1 (5.4)	0.001*
HAD Depression	-2.3 (2.6)	<0.001*	-2.4 (3.8)	0.002*
Breath hold (seconds)	8.5 (8.4)	<0.001*	6.6 (12.6)	0.012*
Cervical flexion right (cm)	6.2 (9.0)	0.001*	7.0 (9.2)	<0.001*
Cervical flexion left (cm)	4.9 (8.3)	0.005*	5.1 (8.3)	0.003*
Bilateral flexion (degrees)	14.9 (21.5)	0.001*	6.9 (20.1)	0.081
Chest expansion (cm)	0.6 (1.3)	0.031*	0.7 (1.0)	0.001*
FEV_1	0.01 (0.31)	0.891	-0.08 (0.14)	0.008*
FVC	0.07 (0.39)	0.334	-0.04 (0.22)	0.339
S_PO_2 pre walk test (%)	0 (1.0)	1.000	0.2 (1.0)	0.383
HR pre walk test (bpm)	-2.9 (8.5)	0.149	-3.9 (8.5)	0.054
Borg Dyspnoea pre walk test	-0.9 (1.6)	0.011*	-0.7 (1.8)	0.059
Borg Fatigue pre walk test	-0.6 (1.2)	0.031*	-0.6 (3.1)	0.336
6MWT distance (m)	31.9 (137.0)	0.256	65.9 (56.7)	<0.001*
Borg Dyspnoea post walk test	-1.4 (1.7)	0.001*	-1.2 (2.1)	0.012*
Borg Fatigue post walk test	-0.9 (2.2)	0.066	-0.9 (2.4)	0.069

Table 3: Within group changes from baseline to final follow up visit

*All values mean (SD). * Indicates statically significant difference.*



264x192mm (96 x 96 DPI)

CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	1
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	2
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	3, 4
	2b	Specific objectives or hypotheses	4
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	4
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	N/A
Participants	4a	Eligibility criteria for participants	4
	4b	Settings and locations where the data were collected	5
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	5
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	5,6
	6b	Any changes to trial outcomes after the trial commenced, with reasons	N/A
Sample size	7a	How sample size was determined	6
	7b	When applicable, explanation of any interim analyses and stopping guidelines	N/A
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	4
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	N/A
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	4
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	4
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those	5

		assessing outcomes) and how	
	11b	If relevant, description of the similarity of interventions	N/A
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	6
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	N/A
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	4, 6, 7
	13b	For each group, losses and exclusions after randomisation, together with reasons	6,7
Recruitment	14a	Dates defining the periods of recruitment and follow-up	6
	14b	Why the trial ended or was stopped	N/A
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	8
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	6
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	9,10,10,11, 12
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	N/A
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	N/A
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	7
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	15
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	16
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	16
Other information			
Registration	23	Registration number and name of trial registry	16
Protocol	24	Where the full trial protocol can be accessed, if available	16
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	16

*We strongly recommend reading this statement in conjunction with the CONSORT 2010 Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see www.consort-statement.org.

CONSORT Flow Diagram