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Title page

Title

Conservative care with or without manipulative therapy in the management of back and/or neck pain in Danish children aged 9-15. A randomized controlled trial nested in a school-based cohort

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Abstract

Objectives: Investigate the effectiveness of adding manipulative therapy to other conservative care for spinal pain in a school-based cohort of Danish children aged 9-15 years.

Design: Two-arm pragmatic randomized controlled trial, nested in a longitudinal open cohort study. Computer-generated block randomization was performed, using a 1:1 allocation to two intervention groups. Due to the nature of the intervention, blinding of the treating chiropractors was not possible. Neither parents nor children were informed about group allocation.

Setting: 13 Danish public schools in the municipality of Svendborg.

Participants: 238 children were randomized individually from February 2012 to April 2014, 116 in the non-manipulative therapy group (49%) and 122 in the manipulative therapy group (51%).

Interventions: Interventions included either 1) advice, exercises, and soft tissue treatment, or 2) advice, exercises, and soft tissue treatment *plus* manipulative therapy.

Outcome measures: The primary outcome was number of recurrences of spinal pain. Secondary outcomes were duration of spinal pain, change in pain intensity, and Global Perceived Effect.

Results: No significant difference was found between groups in the primary outcome (non-manipulative therapy group median 1 (IQR 1-3) and manipulative therapy group median 2 (IQR 0-4), p=0.07). Children in the group receiving manipulative therapy reported a higher Global Perceived Effect: OR 2.22, (95% CI 1.19-4.15). No adverse events were reported.

Conclusions: Adding manipulative therapy to other conservative care in school children with spinal pain did not result in fewer recurrent episodes. The choice of treatment – if any – for spinal pain in children therefore relies on personal preferences, and could include conservative care with and without manipulative therapy. Participants in this trial may differ from a normal care-seeking population.

Trial registration: ClinicalTrials NCT01504698

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Strengths and limitations of this study

- The school-based design minimized social bias and provided equal access for all.
- The prospective open cohort design allowed for a long follow-up period.
- The SMS track system is very efficient in collecting frequent data over a long time.
- The SMS track reflects how often parents reported spinal pain on behalf of the child, but this may not reflect the experience of the child.
- The inclusion criteria of a Numerical Rating Scale score of 3 or more on the day of examination and pain for at least 3 days is probably below the normal pain intensity threshold for seeking treatment.

INTRODUCTION

Today, no 'gold standard' treatment exists for children with spinal pain, i.e. back and/or neck pain[1 2], but manipulative therapy (i.e. joint manipulation and/or mobilization) is increasingly being used despite a lack of evidence of its effectiveness[3-5]. Manipulative therapy is generally recommended as a treatment option for adults with spinal pain[6-9], and is delivered by various health professions, both on its own and in combination with other types of therapy, such as advice, exercises, and soft tissue treatment[3 4 10 11]. Management of children's health relies to a large extent on parents' values, preferences and experience, and in the absence of guidelines for the treatment of spinal pain in children, healthcare professionals have to rely on guidelines developed for adults[6 12]. Although spinal pain is transient and inconsequential for most children, some have frequent and bothersome complaints[13 14] and the prevalence increases with age[14-16]. Furthermore, spinal pain is recurrent in some children[17 18] and spinal pain in adolescence is a strong predictor for similar problems in adulthood[19-21].

The aim of this pragmatic randomized controlled trial (RCT) was to determine the effectiveness of adding manipulative therapy to other conservative care (advice, exercises and soft tissue treatment) on the number of recurrences of spinal pain in children aged 9 to 15 years who were participating in a school-based open cohort study. Secondary outcomes included the short-term effect on duration of spinal pain episodes, pain intensity, and Global Perceived Effect.

METHOD

Study design

A pragmatic parallel observer-blinded RCT nested in a school-based open cohort.

Participants and setting

This study was nested in The Childhood Health, Activity and Motor Performance School Study (CHAMPS Study-DK)[22], which is a Danish longitudinal school-based open cohort study including approximately 1,400 children aged 9 to 15 years from 13 public schools. The CHAMPS Study-DK was an open cohort study hence children could enter or leave the cohort at any time during the study period. The children were followed weekly with text messages (SMS) to one of their parents inquiring, amongst other things, about any musculoskeletal pain the child might have had during the past week (Questions in Supplementary File 1). Data collection on musculoskeletal complaints for this RCT began in February 2012 and ended at the end of June 2014.

Eligibility determination

All children enrolled in the CHAMPS Study-DK were invited to participate in the RCT. The complete protocol for the RCT is described in detail elsewhere[23]. Briefly, when a parent answered positively on the SMS to the presence of spinal pain in their child, a member of a screening team (licensed chiropractors and physiotherapists) telephoned the parent and conducted a standardized interview about the complaint, in order to determine whether the child was eligible for inclusion in the RCT. Initial eligibility was based on: 1) the pain was spinal and still present at the time of the interview, 2) the parent had agreed, on behalf of the child, to join the RCT, and 3) the child had not had

any manual treatment of the spine during the previous 2 months. Within 2 weeks, the child was evaluated at the school by a chiropractor from the RCT team (seven licensed chiropractors) to determine whether he or she fulfilled the inclusion criteria (Table 1).

Table 1 Inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
• Pain in neck or back equal to or greater than 3 on an 11-box numerical rating scale on the day of examination and pain for more than three days	• Serious pathology (cancer, inflammatory diseases, vertebral fractures, cauda equina syndrome)
	• Manual treatment for the past 2 months (for this particular complaint)
	• Handicaps preventing normal physical activity

After the evaluation, both the child and his/her parents were informed about the results and treatment was initiated. The flow from SMS to RCT can be seen Figure 1.

Randomization

A computer-generated block randomization was made with block sizes alternating between two and six at the time of inclusion, using a 1:1 allocation to the two groups. The consecutive designations of the two groups were written on separate pieces of paper and given to the chiropractors in the RCT team in sealed opaque envelopes. A research assistant, who was not otherwise connected to the study, performed the procedure.

First consultation

At the first consultation, the chiropractor obtained a case history, including pain intensity on an 11-box Numerical Rating Scale [24], performed a clinical examination, and

various baseline data were acquired (Supplementary File 2). Two weeks after inclusion, the child was asked about Global Perceived Effect (Supplementary File 3) and pain intensity.

If a child experienced a recurrence of spinal pain or a musculoskeletal complaint in the extremities during the study period (i.e. the parent reported pain on the weekly SMS), the procedure was repeated except for randomization, which was carried forward throughout the study period regardless of the body location in which the complaint occurred. All data were filed in electronic data storage systems established specifically for this project and stored on secure servers.

Interventions

The non-manipulative therapy group (non-MT group) received advice, exercises and, soft tissue treatment, and the manipulative therapy group (MT group) received advice, exercises and, soft tissue treatment *plus* manipulative therapy (Table 2).

Table 2 Intervention groups

The non-manipulative group	The manipulative group received
• Pragmatic advice (activity level, ergonomics, cold packs etc.) • Exercises (stretching and/or strengthening exercises) • Soft tissue treatment (manual trigger point therapy or massage)	• Advice, exercises and soft tissue treatment • Manipulative therapy: joint manipulation and/or mobilization

Manipulative therapy was delivered at the discretion of the chiropractor and applied on the basis of an assessment of biomechanical dysfunction and pain provocation found during clinical examination of the child's spine and extremities[25]. Because of the pragmatic nature of the study, the frequency and content of treatments in both groups was determined by the treating chiropractor at each visit, similar to what is normal in

clinical practice. Because the treatment team consisted of seven chiropractors, a child could be treated by different chiropractors during different appointments. Treatments continued until the child no longer had any symptoms related to the musculoskeletal complaint, or until the chiropractor or parent decided that further treatment was not indicated. The child and/or parents could terminate the treatments or drop out of the RCT at any time during the study period, but still stay in the cohort of the CHAMPS Study-DK.

Blinding

Due to the nature of the intervention, blinding of the treating chiropractors was not possible, however, neither parents nor children were informed about group allocation and parents did not attend treatment sessions and answered the SMS without contact with clinicians or researchers. The coding of the intervention group was not revealed to the primary investigator or the statisticians until after the analyses had been completed.

Outcomes

The primary outcome was the number of recurrences as measured via the weekly SMS messages. A recurrence was defined as a new episode of spinal pain (i.e. back and/or neck pain) occurring after at least 1 week without spinal pain following the end of the previous episode. (See secondary outcomes, Table 2).

Table 2 Outcomes, definitions and statistical methods

Primary outcome	Definition	Statistical method
Number of recurrences of spinal pain (3-27 months follow up)	i) A positive answer on the weekly SMS for spinal pain ii) Minimum of 1 week without report of spinal pain prior to the recurrence	A hierarchical negative binomial regression model with follow-up time included as exposure time was used. Intervention effects were expressed as incidence rate

		ratio
Secondary outcomes		
Average duration of spinal pain episodes	The number of consecutive weeks the child was affected by spinal pain (response option '1')	A mixed effects linear regression model with subject as random effect, outcome log transformed was used. Intervention effects were expressed as the difference in median length
Total duration of complaint time in relation to individual follow-up time	Total number of weeks a child was affected by spinal pain (response option '1') in the entire follow-up period	A hierarchical negative binomial regression model with follow-up time included as exposure time was used. Intervention effects were expressed as incidence rate ratio
Global Perceived Effect after 2 weeks	Dichotomized into two groups: "Much better" and "The same or worse"	A logistic regression model was used. Intervention effects were expressed as odds ratios
Change in pain intensity after 2 weeks	Rated on an 11-point Numerical Rating Scale with '0' being 'no pain' and '10' being 'worst pain'	A linear regression model was used. Intervention effects were expressed as the difference in mean length

Sample size

As the study had continuous inclusion, we continued to recruit participants until 3 months prior to the end of data collection in summer 2014, to include as many participants as possible with varying follow-up times. Based on preliminary analyses, this resulted in a power of 76% for the number of recurrences, 20% for episode length and 87% for overall complaint time[23].

Statistical methods

All analyses used an intention-to-treat approach. Various types of regression analyses were used depending on the type of outcome; follow-up time was included as an

exposure time variable; subject was included as random effect in models with repeated measurements; and class and school were evaluated and included in the models as random effects if their effect was statistically significant (see details, Table 2). No effect was seen on any of the outcomes and hence, cluster was not included in the models. For linear models, means and standard deviations (SD) were used if data were normally distributed; otherwise medians and interquartile ranges (IQR) were reported. All methods were checked according to fulfilment of other assumptions and changed where appropriate. Due to some missing SMS answers, we imputed missing data as follows: if four or fewer consecutive missing answers were preceded and followed by a '1', this was considered as one continuous episode and the missing values were imputed as ´1'[26].

A sensitivity analysis was conducted to assess the effect of the choice of definitions in relation to recurrence and duration. Hence, in this analysis, a new episode was defined to occur after 4 weeks of 'no pain' instead of 1 week before it was considered a new episode.

STATA 14.2 (StataCorp, College Station, Texas, USA) was used for data analyses. Significance level was set to 5%□.

Ethics

All parents gave written informed consent to participation on behalf of the child and the children gave oral consent. A child could be withdrawn from the study at any time during the study period and the study was conducted according to the Declaration of Helsinki. The project was approved by The Regional Committee on Health Research Ethics (#S-20110042) and data were handled according to the regulations set by the Danish Data Protection Agency (#2013-41-1738).

RESULTS

The inclusion period ran from February 1st 2012 to April 1st 2014, and the follow-up period ended on June 27th 2014 (the end of the school year) resulting in between 1 and 868 follow-up days, (mean 477 days; SD 233). A total of 770 children reported spinal pain on SMS, and after telephone interviews, 483 children were evaluated for eligibility but did not fulfil the inclusion criteria. Additionally, 44 individuals reported pain less than 3 on the Numerical Rating Scale on the day of examination, leaving 243 children randomized and enrolled in the study. During data cleaning, we found five participants had been wrongly included, i.e. the SMS answer indicated no spinal pain, and they were excluded from the analyses. Thus, the final cohort for analysis consisted of 238 children with a mean age of 12.6 years: 116 in the non-MT group (49%) and 122 in the MT group (51%), (CONSORT Flow Diagram Figure 2).

Baseline covariates can be seen in Table 3, which also reports the amount of missing data for each variable. There was no difference between the groups for any of the covariates indicating randomization was successful and therefore univariate analyses were performed for all analyses.

Table 3 Baseline data. Baseline covariates by intervention group

	Non-MT group (n=116)	MT group (n=122)	Missing non-MT group*	Missing MT group*
Sex, Female, No (%)	73 (63)	78 (64)		
	Mean (CI)	Mean (CI)		
Age at inclusion	12.6 (12.4-12.9)	12.6 (12.3-12.9)		
Follow up time (days)	492 (448-536)	463 (423-504)		
Pain intensity at baseline (NRS)	5.3 (5.1-5.6)	5.2 (4.9-5.5)		
	Proportion (CI)	Proportion (CI)		
Expectations of the clinical course ("Worse")	7.6% (3.4-16.1)	7.6% (3.4-16.1)	32% (37)	35% (43)
	Median (IQR)	Median (IQR)		

KID Physical wellbeing	44.7 (38.5-49.6)	43.8 (40.5-49.6)	4% (5)	1% (1)
KID Psychological wellbeing	49.5 (44.8-56.0)	48.5 (44.8-56.0)	5% (6)	2% (3)
KID Autonomy and relation	49.5 (45.2-55.8)	49.5 (45.2-55.8)	4% (5)	2% (3)
KID Social support and peers	53.2 (46.9-57.8)	53.2 (46.9-57.8)	4% (5)	1% (1)
KID School	51.1 (45.4-58.2)	51.1 (45.4-54.4)	4% (5)	1% (1)

* Number of children with missing data according to intervention group; Non-MT: non-manipulative therapy; MT: manipulative therapy; CI: confidence intervals; NRS: Numerical Rating Scale; IQR: interquartile range; KID: KIDScreen domains

Primary outcome

During the follow-up period, 175 (74%) of the children had a total of 592 recurrences, ranging from 1 to 21 recurrences per child. The median number of recurrences was 2 (IQR 0-4) for the manipulative therapy group and 1 (IQR 1-3) for the non-manipulative therapy group, revealing no statistically significant difference between groups, incidence rate ratio (IRR) 1.26 (95% CI 0.98-1.61), p=0.07.

Secondary outcomes

We found no significant difference in the average episode length, total number of pain weeks or change in pain intensity between the two groups. Children in the group receiving manipulative therapy reported a higher Global Perceived Effect: odds ratio (OR) 2.22, (95% CI 1.19-4.15), that was statistically significant. All results are displayed in Table 4.

Table 4 Results on secondary outcomes

	MT group	**Non-MT group**
Length of spinal pain episode		
Total number of episodes	456 (55%)	374 (45%)
Median (IQR) (number of weeks)	2 (1-6)	2 (1-5)
β-coefficient (95% CI)	0.11 (-0.07; 0.29)	
P value	0.21	
Total duration of complaint time per child		

Total number of pain weeks	1-114	1-111
Median (IQR)	9 (IQR 4-22)	7 (IQR 4-18)
IRR (95 % CI)	1.16 (0.92-1.48)	
P value	0.22	
Global Perceived Effect		
Number of children in analysis*	96 (52%)	86 (48%)
OR (95% CI)	2.22 (1.19-4.15)	
P value	0.01	
NRS change		
Number of children in analysis*	112 (50%)	111 (50%)
Mean (SD)	2.2 (2.5)	2.3 (2.7)
β-coefficient (95% CI)	0.10 (-0.57; 0.78)	
P value	0.76	

* Number of children in analysis of the first episode due to missing data; IQR: interquartile range; IRR: incidence rate ratio; OR: odds ratio; NRS: Numerical rating Scale; SD: standard deviation

Sensitivity analysis on number of pain free weeks

The number of recurrences declined from a total of 592 to 259 when we defined a new episode to occur after 4 weeks of 'no pain' instead of 1 week. This, however, did not change the between-group difference on either the primary outcome or most of the secondary outcomes, but it did result in a statistically significant increased length of episode for the MT group, mean 3.5 (3.0-4.0) vs. 4.4 weeks (3.8-5.0) and median 2 (1-5) vs. 2 (1-4), P=0.045.

Harms

To our knowledge, no serious harms following manipulative therapy have been reported in children of this age group[27 28]. However, it is common to experience temporary reddening or soreness in the area being treated after both soft tissue treatment and manipulative therapy[29]. Treating chiropractors recorded treatment-related harms if the child stated these at the consultation, but none were reported and no child was referred

to other health care providers, including general practitioners, because of side effects or harms.

DISCUSSION

Adding manipulative therapy to other conservative care for children reporting spinal pain did not result in fewer recurrences in a school-based cohort of Danish children aged 9-15 years. Furthermore, the average episode length, total number of pain weeks, and change in pain intensity were no different between the groups. However, in the sensitivity analyses, filtering out the frequently recurring episodes, the difference for episode length did become statistically significant. Children randomized to the MT group reported a higher Global Perceived Effect that was statistically significant. Thus, no increased effectiveness was evident and no harm was detected.

To our knowledge, this is the first RCT evaluating the added benefit of manipulative therapy in children with spinal pain (i.e. back and/or neck pain). Michaleff et al[2] found only four RCTs dealing with conservative interventions for low back pain in children and all had a high risk of bias. Only one of these included manual therapy combined with exercise, but it had only 45 participants.

Because this study was a two-armed parallel trial with manipulative therapy as an addition to other conservative care, it is probably not surprising that we did not find a large difference between the two groups. This RCT was nested in a large cohort study, and hence we could not prolong the study period to increase the sample size; however, given the small absolute differences found on both primary and secondary outcomes,

this is unlikely to have changed our conclusions. We originally intended to analyse the three spinal regions separately, however the pain site could change within the same individual during follow up, and many individuals reported pain from several regions. Therefore, such an analysis would have been difficult to interpret.

The Numerical Rating Scale has been shown to be a valid tool for assessing pain in children[24 30 31], and in this study, the children also appeared to be able to rate their pain on the scale quite easily. However, when analysing the data, we found that Numerical Rating Scale ratings were not always in accordance with Global Perceived Effect ratings, i.e. some children would say they felt better, although reporting a higher score on the Numerical Rating Scale at follow up than at baseline. This noise may be caused by variation in cognitive abilities and maturity between the children, and is probably equally distributed between groups. Regardless, we did not find statistically significant differences between the groups on change in Numerical Rating Scale scores, and both achieved a mean change of 2.3, which can be regarded as a clinically meaningful change, as studies have shown a minimal clinically important change to be +/- 1[32 33].

We could not find any literature supporting the validity of measures of Global Perceived Effect in children, but validity of this measure has been shown to be good in adults[34 35] and we therefore included it as a measure of the child's own perception of improvement. We would have expected that statistically significant differences between the groups would follow the same pattern for the Numerical Rating Scale and the Global Perceived Effect, but this was not the case. Therefore, the validity of both of these as outcome measures in clinical trials involving children should be further explored.

Strengths and weaknesses

The principal strength of this study was the school-based design, which had a number of advantages: the logistical burden for the parents was reduced because the treatment took place during school time, social bias was likely to be minimal or absent because everybody was invited to participate in the study, and there was equal access because all treatment in the trial was free. Also, this design allowed for a long follow-up period for most children. By nesting this RCT in a school-based cohort, we may however have included children who would not normally have sought care, i.e. likely to have had sub-clinical pain. The inclusion criterion of a Numerical Rating Scale score of 3 or more on the day of examination is probably also below the normal pain intensity threshold for seeking treatment and many parents would probably have waited until the pain had become worse or lasted longer before seeking care. On the other hand, the number and duration of spinal pain episodes were higher in the study sample than in the full cohort (mean number 3.5 versus 2, mean duration 4.6 versus 2.8)[26], suggesting that the children enrolled in this study were more affected by pain than their non-participating peers.

SMS is a very efficient way of collecting frequent data over a long time[36 37]. In this study, the SMS responses were a reflection of how often the parents reported on their child's pain and might not have been a true reflection of how the child actually felt. We know that there is a discrepancy between parent and child reporting of spinal pain[38-40]. Parents appear to under-report compared to their child when pain is at a low level, whereas concordance is higher when the pain is more severe. Thus, it is possible that the parents stopped reporting pain because they assumed the complaint to be minor, even

though the child might still have had pain. This could explain some of the difference between outcomes reported by the children (Global Perceived Effect) and outcome reported by the parents (SMS).

Using different practitioners prevents a potential patient-practitioner relationship and is considered a strength; however, the more people involved, the more irregularities and mistakes are likely to occur. One example of this is the poor response rate to the measures collected by the clinicians, e.g. Numerical Rating Scale and Global Perceived Effect scores.

Missing data

The amount of missing data was substantial for some of the secondary outcomes, and therefore we analysed only those for the first spinal pain episode. However, there was no difference in response rates between groups, and it was assumed that data were missing completely at random and not due to any underlying confounding factors or bias. Possible reasons for missing data could be practitioners' forgetfulness or an electronic system defect resulting in missing data. Because of missing data, we cannot say anything valid about the course of pain, e.g. whether there is a learning effect over time or whether expectations of treatment differ over time between the two groups.

Future research

Since the inclusion criteria in this study were very broad, subgroup analyses would be valuable to inform future studies, i.e. if there are subgroups of children who respond better or worse to manipulative therapy than to other treatments. Future RCTs should include care-seeking children who self-report their response to treatment in order to

evaluate effectiveness in that population. In addition, inclusion of an untreated group would elucidate the effect of treating these children, whether manipulative therapy is included or not.

Conclusion

We found no significant difference in the number of recurrences of episodes of spinal pain in a school-based cohort of children when adding manipulative therapy to advice, exercises, and soft tissue therapy. The study population may not be comparable to a normal care-seeking population and therefore the results may not be directly transferrable.

Author Contributions

All authors (KBD, JH, NW, LH) participated in conceptualising and designing this study, as well as designing and interpreting the analyses of the study. Kristina Boe Dissing was project manager for the trial, performed the analyses and drafted the initial manuscript. All authors (KBD, JH, NW, LH) reviewed and revised the manuscript and approved the final version of the manuscript.

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Competing interests

The authors have no competing interests to declare.

Data sharing statement

Data are from the Childhood Health, Activity and Motor Performance School Study (CHAMPS Study-DK) and are available on request from the project manager Niels Wedderkopp.

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Figure legends

Figure 1 Flow from SMS to RCT.

RCT: randomised controlled trial. SMS: text message. MT group: manipulative therapy group. Non-MT group: non-manipulative therapy group

Figure 2 CONSORT Flow Diagram

Supplementary Files

Supplementary File 1. SMS questions

Supplementary File 2. Covariates, baseline data and definitions

Supplementary File 3. Global perceived effect question

CONSORT checklist

Study protocol

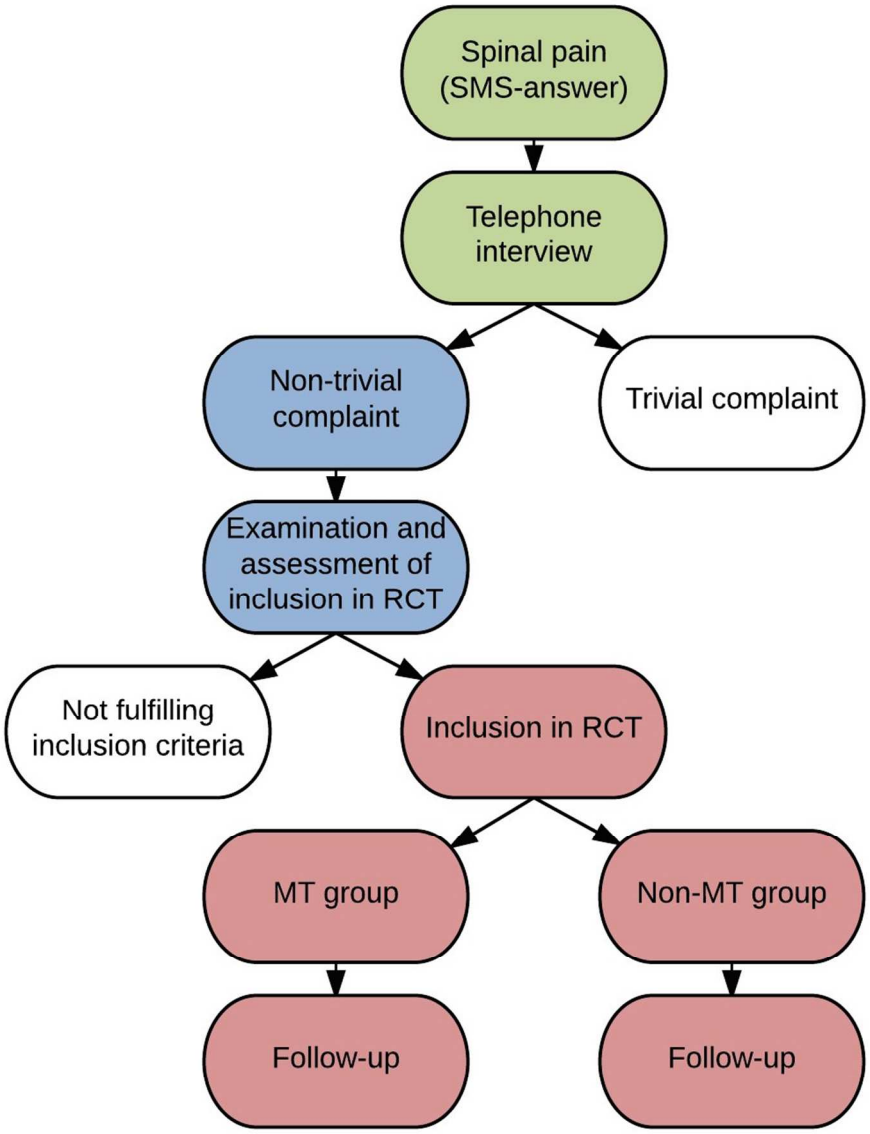

Figure 1 Flow from SMS to RCT

85x115mm (300 x 300 DPI)

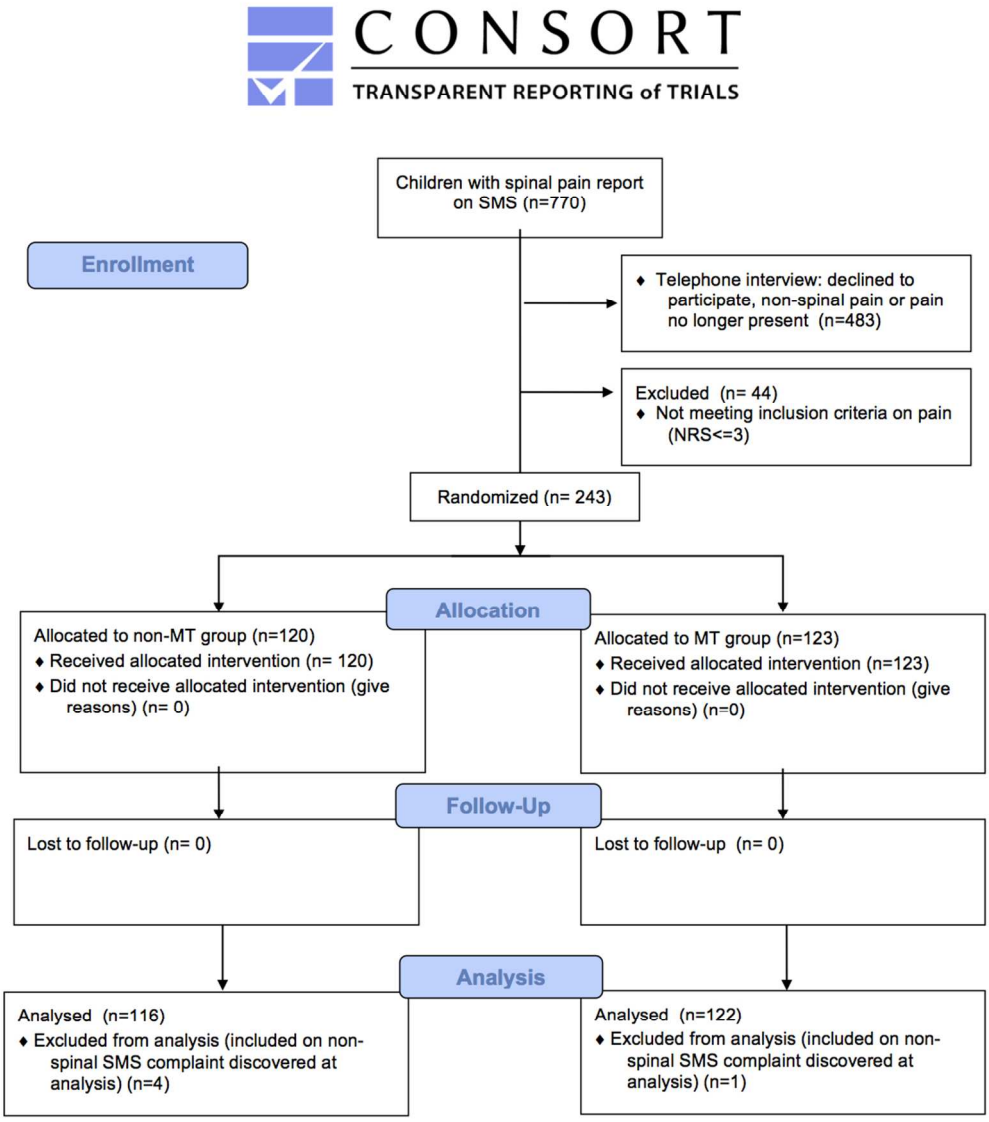

Figure 2 CONSORT Flow Diagram

97x110mm (300 x 300 DPI)

Supplementary File 1

SMS questions

1. **Has <FIRSTNAME> had pain for the last week?**

1.Neck, back or lumbar spine
2.Shoulder, arm or hand
3.Hip, leg or foot
4.No, my child has not had any pain

2. **How many times has <FIRSTNAME> been to organized sports in his/her leisure time in the past week?**

0 = 0 times
1 = 1
2 = 2
3 = 3
4 = 4
5 = 5
6 = 6
7 = 7
8 = more than 7 times

3. **<FIRSTNAME> which kinds of sports?**

1 Soccer
2 Handball
3 Basketball
4 Volleyball
5 Gymnastics
6 Tumbling
7 Swimming
8 Horse back riding
9 Dancing
10 Other

Supplementary File 2. Covariates, baseline data and definitions

Covariates	**Definitions**
KIDSCREEN 27 questionnaire	Quality of life measured from 27 questions covering the following five domains. Values vary from 10-70 with population norm mean=50, high value equals better QOL
KID Physical	Physical wellbeing domain
KID Psych	Psychological wellbeing domain
KID Autonomy	Autonomy and parent relation domain
KID Social	Social support and peers domain
KID School	School domain
Expectations of the clinical course (EoCC)	The child was asked before the treatment: "What do you expect the outcome of your spinal pain will be compared with how it is now?" Rated on a 5-point scale ('1' being 'much worse' and '5' being 'much better')
Baseline data	
Age	9-15 years
Sex	Boy/girl
Intervention group	Manipulative group/non-manipulative group
School	13 schools included (used as cluster)
Class	4th to 9th grade (used as cluster)

Supplementary File 3

Global perceived effect

Name:
Id number:

Date:

How will you describe your general wellbeing now in your neck/back (and any extremities) as opposed to 2 weeks ago before treatment was started?

(Only one tick in the following)

- Much better
- Better
- Little better
- Almost the same
- Little worse
- Worse
- Much worse

Rated in the file from 1-7, with 1 being much better and 7 being much worse.

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)	3
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	5
	2b	Specific objectives or hypotheses	5
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	6
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	
Participants	4a	Eligibility criteria for participants	6-7
	4b	Settings and locations where the data were collected	6
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	8-9
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	9-10
	6b	Any changes to trial outcomes after the trial commenced, with reasons	16
Sample size	7a	How sample size was determined	10
	7b	When applicable, explanation of any interim analyses and stopping guidelines	
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	7
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	7
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	7
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	7
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those	9

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

*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.

BMJ Open

Conservative care with or without manipulative therapy in the management of back and/or neck pain in Danish children aged 9-15: a randomized controlled trial nested in a school-based cohort

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Title page

Title

Conservative care with or without manipulative therapy in the management of back and/or neck pain in Danish children aged 9-15: a randomized controlled trial nested in a school-based cohort

Short title: Manipulative therapy and children

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Abstract

Background

A substantial number of children experience spinal pain, i.e. back and/or neck pain. Today, no 'gold standard' treatment for spinal pain in children exists, but manipulative therapy is increasingly being used in spite of a lack of evidence of its effectiveness. This study investigates the effectiveness of adding manipulative therapy to other conservative care for spinal pain in a school-based cohort of Danish children aged 9-15 years.

Methods and Findings.

The design was a two-arm pragmatic randomized controlled trial, nested in a longitudinal open cohort study in Danish public schools. 238 children from 13 public schools were randomized individually from February 2012 to April 2014. A text message system and clinical examinations were used for data collection. Interventions included either 1) advice, exercises, and soft tissue treatment, or 2) advice, exercises, and soft tissue treatment *plus* manipulative therapy. The primary outcome was number of recurrences of spinal pain. Secondary outcomes were duration of spinal pain, change in pain intensity, and Global Perceived Effect.

We found no significant difference between groups in the primary outcome (control group median 1 (IQR 1-3) and intervention group 2 (IQR 0-4), p=0.07). Children in the group receiving manipulative therapy reported a higher Global Perceived Effect: OR 2.22, (95% CI 1.19-4.15). No adverse events were reported. Main limitations are the potential discrepancy between parental and child reporting and that the study population may not be comparable to a normal care-seeking population.

Conclusions

Adding manipulative therapy to other conservative care in school children with spinal pain did not result in fewer recurrent episodes. The choice of treatment – if any – for spinal pain in children therefore relies on personal preferences, and could include conservative care with and without manipulative therapy. Participants in this trial may differ from a normal care-seeking population.

Trial registration: ClinicalTrials NCT01504698

Key words: randomized controlled trial, children, adolescents, spinal pain, back pain, neck pain, manipulative therapy

Strengths and limitations

- The school-based design minimized social bias and provided equal access for all.
- The prospective open cohort design allowed for a long follow-up period.
- The SMS track system is very efficient in collecting frequent data over a long time.
- The SMS track reflects how often parents reported spinal pain on behalf of the child, but this may not reflect the experience of the child.
- The inclusion criteria of a Numerical Rating Scale score of 3 or more on the day of examination and pain for at least 3 days is probably below the normal pain intensity threshold for seeking treatment.

INTRODUCTION

Spinal pain is prevalent in youth and reaches adult levels already around the age of 18[1], but it is transient and inconsequential for most children. Therefore it has largely been ignored in research, but some children have frequent, recurrent and bothersome complaints[2-5], which impact mental wellbeing[6] and have the potential to decrease the level of physical activity. Importantly, these problems seem to track into adulthood, i.e. the most affected adolescents grow up to be the most affected adults[7 8]. Therefore, proper management at an early stage is essential to improve lifetime trajectories of spinal pain.

Management of children's musculoskeletal disorders relies to a large extent on parents' values, preferences and experience, and due to absence of guidelines for the treatment of spinal pain in children, healthcare professionals have to rely on guidelines developed for adults[9].

Manipulative therapy (MT) is defined as joint manipulation and/or mobilization with the aim to restore compromised function of joints[10]. This type of therapy is increasingly being used in children[11-13] because it is generally recommended as a treatment option for adults with spinal pain[14-18], and is delivered by various health professions, both on its own and in combination with other types of therapy, such as advice, exercises, and soft tissue treatment[18]. One study recently demonstrated a small but statistically significant effect of adding SMT to exercise therapy[19] in adolescents with low back pain. However this is the only full scale randomized controlled trial (RCT) conducted to date to investigate the effect of SMT in children with any type of spinal pain[9 20].

The aim of this pragmatic randomized controlled trial was to determine the effectiveness of adding manipulative therapy to other conservative care (advice, exercises and soft tissue treatment) on the number of recurrences of spinal pain in children aged 9 to 15 years who were participating in a school-based open cohort study. Secondary outcomes included the short-term effect on duration of spinal pain episodes, pain intensity, and Global Perceived Effect.

METHOD

Study design

A pragmatic parallel observer-blinded RCT nested in a school-based open cohort.

Participants and setting

This study was nested in The Childhood Health, Activity and Motor Performance School Study (CHAMPS Study-DK)[21], which is a Danish longitudinal school-based open cohort study including approximately 1,400 children aged 9 to 15 years from 13 public schools. The CHAMPS Study-DK was an open cohort study hence children could enter or leave the cohort at any time during the study period. The children were followed weekly with text messages (SMS) to one of their parents inquiring, amongst other things, about any musculoskeletal pain the child might have had during the past week (Questions in Supplementary File 1). Data collection on musculoskeletal complaints for this RCT began in February 2012 and ended at the end of June 2014.

Eligibility determination

All children enrolled in the CHAMPS Study-DK were invited to participate in the RCT. The complete protocol for the RCT is described in detail elsewhere[22]. Briefly, when a parent answered positively on the SMS to the presence of spinal pain in their child, a member of a screening team (licensed chiropractors and physiotherapists) telephoned the parent and conducted a standardized interview about the complaint, in order to determine whether the child was eligible for inclusion in the RCT. Initial eligibility was based on: 1) the pain was spinal and still present at the time of the interview, 2) the parent had agreed, on behalf of the child, to join the RCT, and 3) the child had not had any manual treatment of the spine during the previous 2 months. Within 2 weeks, the child was evaluated at the school by a chiropractor from the RCT team (seven licensed chiropractors) to determine whether he or she fulfilled the inclusion criteria (Table 1).

Table 1 Inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
• Pain in neck or back equal to or greater than 3 on an 11-box numerical rating scale for more than three days indicated by the child at the first visit	• Serious pathology (cancer, inflammatory diseases, vertebral fractures, cauda equina syndrome)
	• Manual treatment for the past 2 months (for this particular complaint)
	• Handicaps preventing normal physical activity

After the evaluation, both the child and his/her parents were informed about the results and treatment was initiated. The flow from SMS to RCT can be seen Figure 1.

Randomization

A computer-generated block randomization was made with block sizes alternating

between two and six at the time of inclusion, using a 1:1 allocation to the two groups. The consecutive designations of the two groups were written on separate pieces of paper and given to the chiropractors in the RCT team in sealed opaque envelopes. A research assistant, who was not otherwise connected to the study, performed the procedure.

First consultation

At the first consultation, the chiropractor obtained a case history, including pain intensity on an 11-box Numerical Rating Scale [23], performed a clinical examination, and various baseline data were acquired (Supplementary File 2). Two weeks after inclusion, the child was asked about Global Perceived Effect (Supplementary File 3) and pain intensity.

If a child experienced a recurrence of pain (i.e. the parent reported pain on the weekly SMS), the procedure was repeated except for randomization, which was carried forward throughout the study period regardless of the body location in which the complaint occurred. All data were filed in electronic data storage systems established specifically for this project and stored on secure servers.

Interventions

The non-manipulative therapy group (non-MT group) received advice, exercises and, soft tissue treatment, and the manipulative therapy group (MT group) received advice, exercises and, soft tissue treatment *plus* manipulative therapy (Table 2).

Table 2 Intervention groups

The non-manipulative group	The manipulative group received
• Pragmatic advice (activity level, ergonomics, cold packs etc.)	• Advice, exercises and soft tissue treatment

• Exercises (stretching and/or strengthening exercises) • Soft tissue treatment (manual trigger point therapy or massage)	• Manipulative therapy: joint manipulation and/or mobilization

Both groups were treated by the RCT team consisting of seven chiropractors. Manipulative therapy was defined as high velocity, low amplitude manipulation and/or mobilization of the joints to restore segmental spinal motion[10]. This was delivered at the discretion of the chiropractor and applied on the basis of a combination of biomechanical dysfunction and pain provocation responses found during the clinical examination of the child[10], since palpatory findings by itself have been found unreliable[24]. If the child experienced any pain in the extremities during the study period, these were also treated with manipulative therapy at the discretion of the treating chiropractor. Because of the pragmatic nature of the study, the frequency and content of treatments in both groups was determined by the treating chiropractor at each visit, similar to what is normal in clinical practice. Because the RCT team consisted of seven chiropractors, a child could be treated by different chiropractors during different appointments. Treatments continued until the child no longer had any symptoms related to the musculoskeletal complaint, or until the chiropractor or parent decided that further treatment was not indicated. The child and/or parents could terminate the treatments or drop out of the RCT at any time during the study period, but still stay in the cohort of the CHAMPS Study-DK.

Blinding

Due to the nature of the intervention, blinding of the treating chiropractors was not possible, however, neither parents nor children were informed about group allocation

and parents did not attend treatment sessions and answered the SMS without contact with clinicians or researchers. The coding of the intervention group was not revealed to the primary investigator or the statisticians until after the analyses had been completed.

Outcomes

The primary outcome was the number of recurrences as measured via the weekly SMS messages. A recurrence was defined as a new episode of spinal pain (i.e. back and/or neck pain) occurring after at least 1 week without spinal pain following the end of the previous episode. (See secondary outcomes, Table 3).

Table 3 Outcomes, definitions and statistical methods

Primary outcome	**Definition**	**Statistical method**
Number of recurrences of spinal pain (3-27 months follow up)	i) A positive answer on the weekly SMS for spinal pain ii) Minimum of 1 week without report of spinal pain prior to the recurrence	A hierarchical negative binomial regression model was used. Intervention effects were expressed as incidence rate ratio
Secondary outcomes		
Average duration of spinal pain episodes	The number of consecutive weeks the child was affected by spinal pain (response option '1')	A mixed effects linear regression model with subject as random effect, outcome log transformed was used. Intervention effects were expressed as the difference in median length
Total duration of complaint time in relation to individual follow-up time	Total number of weeks a child was affected by spinal pain (response option '1') in the entire follow-up period	A hierarchical negative binomial regression model was used. Intervention effects were expressed as incidence rate ratio
Global Perceived Effect after 2 weeks	Dichotomized into two groups: "Much better" and "The same or worse"	A logistic regression model was used. Intervention effects were expressed as odds ratios
Change in pain intensity after 2 weeks	Rated on an 11-point Numerical Rating Scale with	A linear regression model was used.

	'0' being 'no pain' and '10' being 'worst pain'	Intervention effects were expressed as the difference in mean length

Sample size

As the study had continuous inclusion, we continued to recruit participants until 3 months prior to the end of data collection in summer 2014, to include as many participants as possible with varying follow-up times. Based on preliminary analyses, this resulted in a power of 76% for the number of recurrences, 20% for episode length and 87% for overall complaint time[22].

Statistical methods

All analyses used an intention-to-treat approach. Various types of regression analyses were used depending on the type of outcome; follow-up time was included as an exposure time variable; subject was included as random effect in models with repeated measurements; and class and school were evaluated and included in the models as random effects if their effect was statistically significant (see details, Table 3). No effect was seen on any of the outcomes and hence, cluster was not included in the models. For linear models, means and standard deviations (SD) were used if data were normally distributed; otherwise medians and interquartile ranges (IQR) were reported. All methods were checked according to fulfilment of other assumptions and changed where appropriate. Due to some missing SMS answers, we imputed missing data as follows: if four or fewer consecutive missing answers were preceded and followed by a '1', this was considered as one continuous episode and the missing values were imputed as ´1'[3]. Since this type of outcome measure has not been used in previous trials, there is no consensus on how to substitute data. In a previous article we have described the

consequences of different data substitution strategies[3].

A sensitivity analysis was conducted to assess the effect of the choice of definitions in relation to recurrence and duration in the present study. In this analysis, a new episode was defined to occur after 4 weeks of 'no pain' instead of 1 week before it was considered a new episode.

STATA 14.2 (StataCorp, College Station, Texas, USA) was used for data analyses. Significance level was set to 5%.

Ethics

All parents gave written informed consent to participation on behalf of the child and the children gave oral consent. A child could be withdrawn from the study at any time during the study period and the study was conducted according to the Declaration of Helsinki. The project was approved by The Regional Committee on Health Research Ethics (#S-20110042) and data were handled according to the regulations set by the Danish Data Protection Agency (#2013-41-1738).

Patient and Public Involvement

There was no patient involvement in the formulation of the research question, the choice of outcome measures, the design, the recruitment procedures, conduct of the study or assessment of the burden of the intervention.

Parents of the included children will receive information about the study and its results via newsletters and the project's website.

RESULTS

The inclusion period ran from February 1st 2012 to April 1st 2014, and the follow-up period ended on June 27th 2014 (the end of the school year). Follow-up time was defined as "Number of days between inclusion date and last SMS". Since one child left the study the day after inclusion, this resulted in 1 to 868 follow-up days, (mean 477 days; SD 233). A total of 770 children reported spinal pain on SMS, and after telephone interviews, 483 children were evaluated for eligibility but did not fulfil the inclusion criteria. Additionally, 44 individuals reported pain less than 3 on the Numerical Rating Scale on the day of examination, leaving 243 children randomized and enrolled in the study. During data cleaning, we found five participants had been wrongly included, i.e. the SMS answer indicated no spinal pain, and they were excluded from the analyses. Thus, the final cohort for analysis consisted of 238 children with a mean age of 12.6 years: 116 in the non-MT group (49%) and 122 in the MT group (51%), (CONSORT Flow Diagram Fig 2).

Baseline covariates can be seen in Table 4, which also reports the amount of missing data for each variable. There was no difference between the groups for any of the covariates indicating randomization was successful and therefore univariate analyses were performed for all analyses.

Table 4 Baseline data. Baseline covariates by intervention group

	Non-MT group (n=116)	MT group (n=122)	Missing non-MT group*	Missing MT group*
Sex, Female, No (%)	73 (63)	78 (64)		
	Mean (CI)	Mean (CI)		
Age at inclusion	12.6 (12.4-12.9)	12.6 (12.3-12.9)		
Follow up time (days)	492 (448-536)	463 (423-504)		
Pain intensity at baseline (NRS)	5.3 (5.1-5.6)	5.2 (4.9-5.5)		

	Proportion (CI)	Proportion (CI)		
Expectations of the clinical course ("Worse")	7.6% (3.4-16.1)	7.6% (3.4-16.1)	32% (37)	35% (43)
	Median (IQR)	Median (IQR)		
KID Physical wellbeing	44.7 (38.5-49.6)	43.8 (40.5-49.6)	4% (5)	1% (1)
KID Psychological wellbeing	49.5 (44.8-56.0)	48.5 (44.8-56.0)	5% (6)	2% (3)
KID Autonomy and relation	49.5 (45.2-55.8)	49.5 (45.2-55.8)	4% (5)	2% (3)
KID Social support and peers	53.2 (46.9-57.8)	53.2 (46.9-57.8)	4% (5)	1% (1)
KID School	51.1 (45.4-58.2)	51.1 (45.4-54.4)	4% (5)	1% (1)

* Number of children with missing data according to intervention group; Non-MT: non-manipulative therapy; MT: manipulative therapy; CI: confidence intervals; NRS: Numerical Rating Scale; IQR: interquartile range; KID: KIDScreen domains

Primary outcome

During the follow-up period, 175 (74%) of the children had a total of 592 recurrences, ranging from 1 to 21 recurrences per child. The median number of recurrences was 2 (IQR 0-4) for the manipulative therapy group and 1 (IQR 1-3) for the non-manipulative therapy group, revealing no statistically significant difference between groups, incidence rate ratio (IRR) 1.26 (95% CI 0.98-1.61), p=0.07.

Secondary outcomes

We found no significant difference in the average episode length, total number of pain weeks or change in pain intensity between the two groups. Children in the group receiving manipulative therapy reported a higher Global Perceived Effect: odds ratio (OR) 2.22, (95% CI 1.19-4.15), that was statistically significant. All results are displayed in Table 5.

Table 5 Results on secondary outcomes

	MT group	**Non-MT group**
Length of spinal pain episode		
Total number of episodes	456 (55%)	374 (45%)
Median (IQR) (number of weeks)	2 (1-6)	2 (1-5)

β-coefficient (95% CI)	0.11 (-0.07; 0.29)	
P value	0.21	
Total duration of complaint time per child		
Total number of pain weeks	1-114	1-111
Median (IQR)	9 (IQR 4-22)	7 (IQR 4-18)
IRR (95 % CI)	1.16 (0.92-1.48)	
P value	0.22	
Global Perceived Effect		
Number of children in analysis*	96 (52%)	86 (48%)
OR (95% CI)	2.22 (1.19-4.15)	
P value	0.01	
NRS change		
Number of children in analysis*	112 (50%)	111 (50%)
Mean (SD)	2.2 (2.5)	2.3 (2.7)
β-coefficient (95% CI)	0.10 (-0.57; 0.78)	
P value	0.76	

* Number of children in analysis of the first episode due to missing data; IQR: interquartile range; IRR: incidence rate ratio; OR: odds ratio; NRS: Numerical rating Scale; SD: standard deviation

Sensitivity analysis on number of pain free weeks

The number of recurrences declined from a total of 592 to 259 when we defined a new episode to occur after 4 weeks of 'no pain' instead of 1 week. This, however, did not change the between-group difference on either the primary outcome or most of the secondary outcomes, but it did result in a statistically significant increased length of episode for the MT group, mean 3.5 (3.0-4.0) vs. 4.4 weeks (3.8-5.0) and median 2 (1-5) vs. 2 (1-4), P=0.045.

Harms

Adverse events can be defined as the sequelae following manipulative therapy to the spine that are medium to long term in duration, with moderate to severe symptoms, and of a nature that is serious, distressing and unacceptable to the patient and requires further treatment[25] To our knowledge, no adverse events following manipulative

therapy have been reported in children of this age group[26 27]. However, it is common to experience transient side effects such as temporary reddening or soreness in the area being treated after both soft tissue treatment and manipulative therapy[28]. Treating chiropractors recorded transient side effects if the child stated these at the consultation, but none were reported and no child was referred to other health care providers, including general practitioners, because of adverse events.

DISCUSSION

Adding manipulative therapy to other conservative care for children reporting spinal pain did not result in fewer recurrences in a school-based cohort of Danish children aged 9-15 years. Furthermore, the average episode length, total number of pain weeks, and change in pain intensity were no different between the groups. However, in the sensitivity analyses, filtering out the frequently recurring episodes, the difference for episode length did become statistically significant. Children randomized to the MT group reported a higher Global Perceived Effect that was statistically significant. Thus, no increased effectiveness was evident and no harm was detected.

To our knowledge, this is the first RCT evaluating the added benefit of manipulative therapy in children with spinal pain (i.e. back and/or neck pain). Michaleff et al[29] found only four RCTs dealing with conservative interventions for low back pain in children and all had a high risk of bias. Only one of these included manual therapy combined with exercise, but it had only 45 participants.

Because this study was a two-armed parallel trial with manipulative therapy as an

addition to other conservative care, it is probably not surprising that we did not find a large difference between the two groups. This RCT was nested in a large cohort study, and hence we could not prolong the study period to increase the sample size; however, given the small absolute differences found on both primary and secondary outcomes, this is unlikely to have changed our conclusions.

Choice of outcomes

We originally intended to analyze the three spinal regions separately, however the pain site could change within the same individual during follow up, and many individuals reported pain from several regions. Therefore, the interpretation of our results relate to 'spinal pain' as a coherent entity. We could not determine by the SMS answers whether recurrences were actual recurrences of the same problem at the same location in the spine, but simply conclude that there was subsequent spine-related pain. This can be considered a weakness as we cannot determine true recurrences; however it can also be considered to be a strength because pain in this age group appears to demonstrate a shift between regions of the spine over time, indicating that there is not independence between pain in the three regions[2]

The Numerical Rating Scale has been shown to be a valid tool for assessing pain in children[23 30 31], and in this study, the children also appeared to be able to rate their pain on the scale quite easily. However, when analyzing the data, we found that Numerical Rating Scale ratings were not always in accordance with Global Perceived Effect ratings, i.e. some children would say they felt better, although reporting a higher score on the Numerical Rating Scale at follow up than at baseline. This noise may be caused by variation in cognitive abilities and maturity between the children, and is probably

equally distributed between groups. Regardless, we did not find statistically significant differences between the groups on change in Numerical Rating Scale scores, and both achieved a mean change of 2.3, which can be regarded as a clinically meaningful change, as studies have shown a minimal clinically important change to be +/- 1[32 33].

We could not find any literature supporting the validity of measures of Global Perceived Effect in children, but validity of this measure has been shown to be good in adults[34 35] and we therefore included it as a measure of the child's own perception of improvement. We would have expected that statistically significant differences between the groups would follow the same pattern for the Numerical Rating Scale and the Global Perceived Effect, but this was not the case. Therefore, the validity of both of these as outcome measures in clinical trials involving children should be further explored.

Strengths and weaknesses

The principal strength of this study was the school-based design, which had a number of advantages: the logistical burden for the parents was reduced because the treatment took place during school time, social bias was likely to be minimal or absent because everybody was invited to participate in the study, and there was equal access because all treatment in the trial was free. Also, this design allowed for a long follow-up period for most children. By nesting this RCT in a school-based cohort, we may however have included children who would not normally have sought care, i.e. likely to have had sub-clinical pain. The inclusion criterion of a Numerical Rating Scale score of 3 or more on the day of examination is probably also below the normal pain intensity threshold for seeking treatment and many parents would probably have waited until the pain had

become worse or lasted longer before seeking care. On the other hand, the number and duration of spinal pain episodes were higher in the study sample than in the full cohort (mean number 3.5 versus 2, mean duration 4.6 versus 2.8)[36], suggesting that the children enrolled in this study were more affected by pain than their non-participating peers.

SMS is a very efficient way of collecting frequent data over a long time[37 38]. In this study, the SMS responses were a reflection of how often the parents reported on their child's pain and might not have been a true reflection of how the child actually felt. We know that there is a discrepancy between parent and child reporting of spinal pain[39-41]. Parents appear to under-report compared to their child when pain is at a low level, whereas concordance is higher when the pain is more severe. Thus, it is possible that the parents stopped reporting pain because they assumed the complaint to be minor, even though the child might still have had pain. This could explain some of the difference between outcomes reported by the children (Global Perceived Effect) and outcome reported by the parents (SMS).

Using different practitioners prevents a potential patient-practitioner relationship and is considered a strength; however, the more people involved, the more irregularities and mistakes are likely to occur. One example of this is the poor response rate to the measures collected by the clinicians, e.g. Numerical Rating Scale and Global Perceived Effect scores.

Missing data

The amount of missing data was substantial for some of the secondary outcomes, and therefore we analyzed only those for the first spinal pain episode. However, there was no difference in response rates between groups, and it was assumed that data were missing completely at random and not due to any underlying confounding factors or bias. Possible reasons for missing data could be practitioners' forgetfulness or an electronic system defect resulting in missing data. Because of missing data, we cannot say anything valid about the course of pain, e.g. whether there is a learning effect over time or whether expectations of treatment differ over time between the two groups.

Future research

Since the inclusion criteria in this study were very broad, subgroup analyses would be valuable to inform future studies, i.e. if there are subgroups of children who respond better or worse to manipulative therapy than to other treatments. Future RCTs should include care-seeking children who self-report their response to treatment in order to evaluate effectiveness in that population. In addition, inclusion of an untreated group would elucidate the effect of treating these children, whether manipulative therapy is included or not.

Conclusion

We found no significant difference in the number of recurrences of episodes of spinal pain in a school-based cohort of children when adding manipulative therapy to advice, exercises, and soft tissue therapy. The study population may not be comparable to a normal care-seeking population and therefore the results may not be directly transferrable.

Authors' contributions

All authors (KBD, JH, NW, LH) participated in the design and interpretation of analyses of this study. Kristina Boe Dissing was project manager for the trial and drafted the manuscript. All authors (KBD, JH, NW, LH) contributed with revisions and approved the final version of the manuscript.

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Competing interests

The authors have no competing interests to declare.

Data sharing statement

Data are from the Childhood Health, Activity and Motor Performance School Study (CHAMPS Study-DK) and are available on request from the project manager Niels Wedderkopp

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Figure legends

Figure 1 Flow from SMS to RCT.

RCT: randomised controlled trial. SMS: text message. MT group: manipulative therapy group. Non-MT group: non-manipulative therapy group

Figure 2 CONSORT Flow Diagram

Supporting information

Supplementary File 1. SMS questions

Supplementary File 2. Covariates, baseline data and definitions

Supplementary File 3. Global perceived effect question

CONSORT checklist

Study protocol

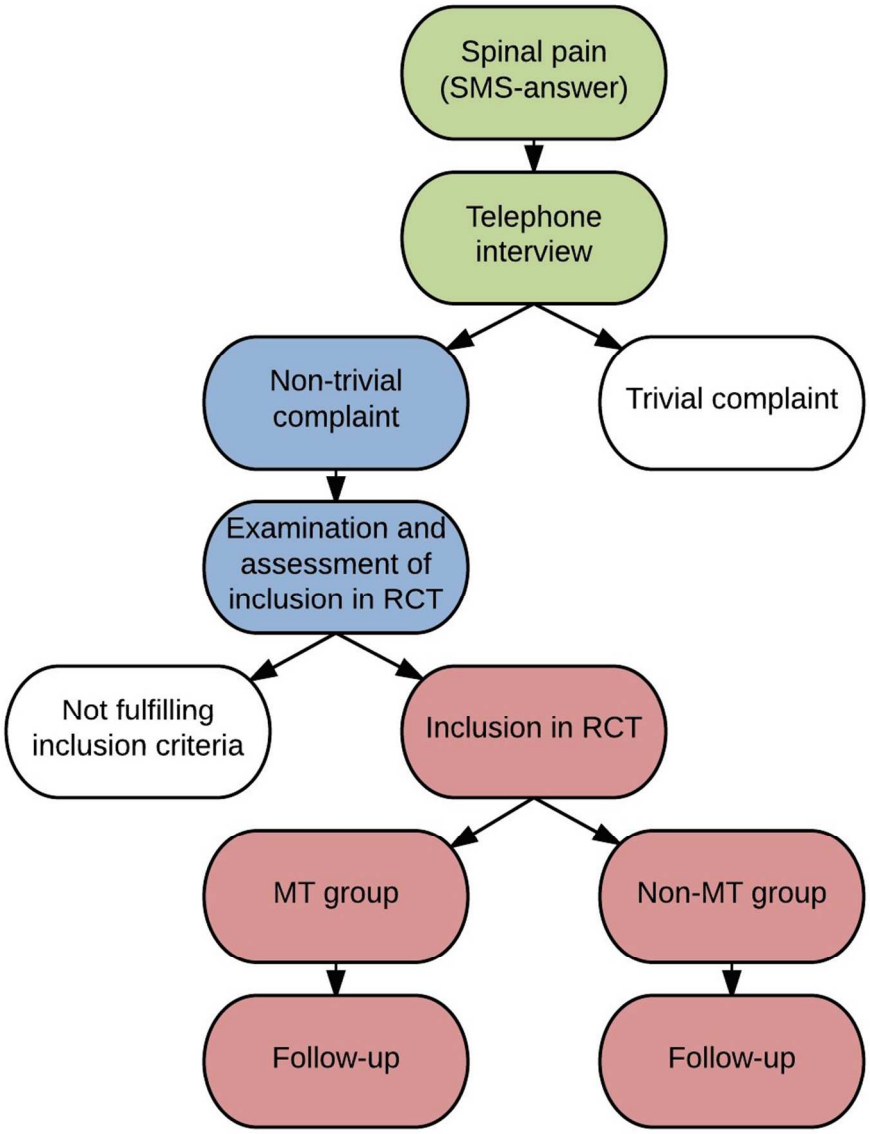

Figure 1 Flow from SMS to RCT

85x115mm (300 x 300 DPI)

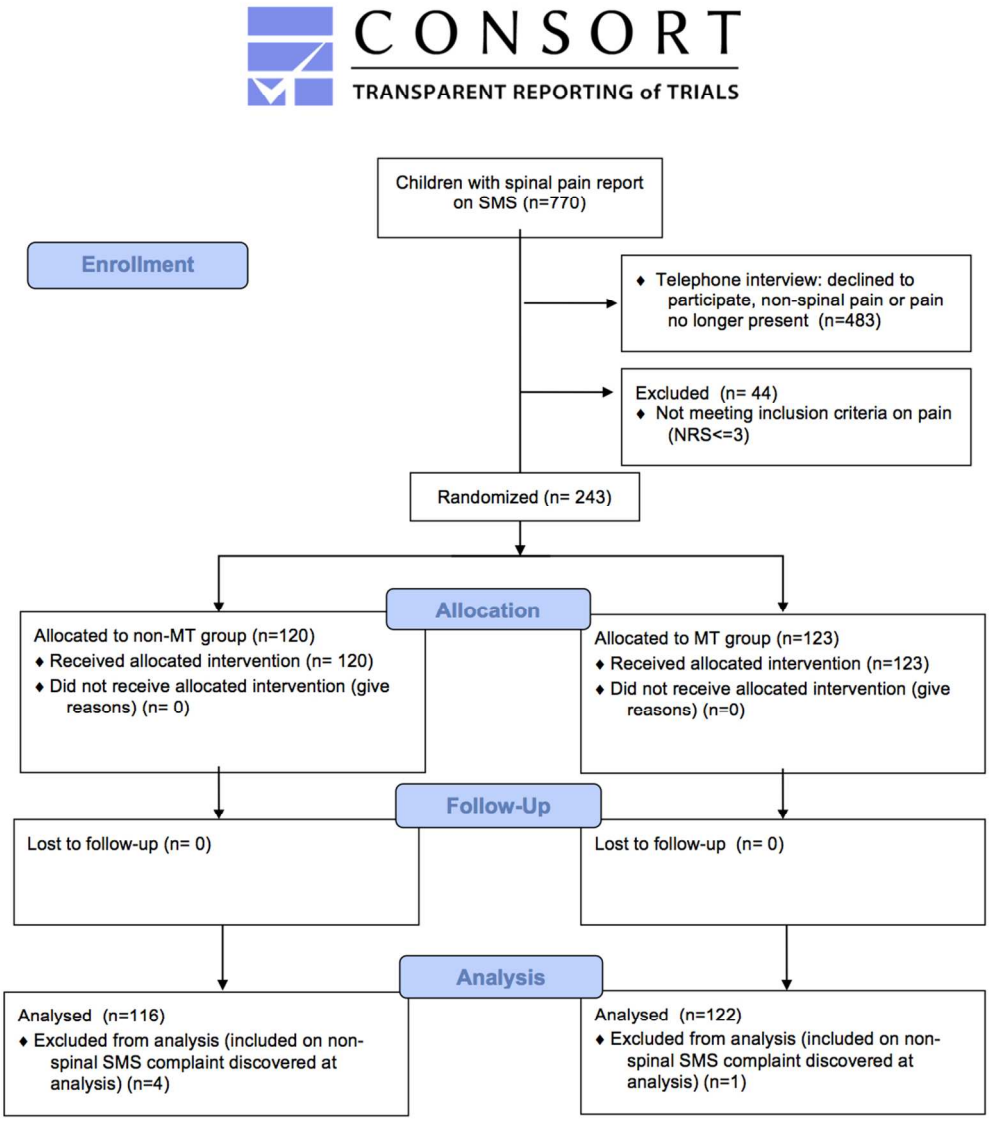

Figure 2 CONSORT Flow Diagram

97x110mm (300 x 300 DPI)

Supplementary File 1

SMS questions

1. **Has <FIRSTNAME> had pain for the last week?**

1.Neck, back or lumbar spine
2.Shoulder, arm or hand
3.Hip, leg or foot
4.No, my child has not had any pain

2. **How many times has <FIRSTNAME> been to organized sports in his/her leisure time in the past week?**

0 = 0 times
1 = 1
2 = 2
3 = 3
4 = 4
5 = 5
6 = 6
7 = 7
8 = more than 7 times

3. **<FIRSTNAME> which kinds of sports?**

1 Soccer
2 Handball
3 Basketball
4 Volleyball
5 Gymnastics
6 Tumbling
7 Swimming
8 Horse back riding
9 Dancing
10 Other

Supplementary File 2. Covariates, baseline data and definitions

Covariates	**Definitions**
KIDSCREEN 27 questionnaire	Quality of life measured from 27 questions covering the following five domains. Values vary from 10-70 with population norm mean=50, high value equals better QOL
KID Physical	Physical wellbeing domain
KID Psych	Psychological wellbeing domain
KID Autonomy	Autonomy and parent relation domain
KID Social	Social support and peers domain
KID School	School domain
Expectations of the clinical course (EoCC)	The child was asked before the treatment: "What do you expect the outcome of your spinal pain will be compared with how it is now?" Rated on a 5-point scale ('1' being 'much worse' and '5' being 'much better')
Baseline data	
Age	9-15 years
Sex	Boy/girl
Intervention group	Manipulative group/non-manipulative group
School	13 schools included (used as cluster)
Class	4th to 9th grade (used as cluster)

Supplementary File 3

Global perceived effect

Name:
Id number:

Date:

How will you describe your general wellbeing now in your neck/back (and any extremities) as opposed to 2 weeks ago before treatment was started?

(Only one tick in the following)

- Much better
- Better
- Little better
- Almost the same
- Little worse
- Worse
- Much worse

Rated in the file from 1-7, with 1 being much better and 7 being much worse.

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)	3
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	5
	2b	Specific objectives or hypotheses	5
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	6
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	
Participants	4a	Eligibility criteria for participants	6-7
	4b	Settings and locations where the data were collected	6
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	8-9
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	9-10
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Sample size	7a	How sample size was determined	10
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*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.

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Conservative care with or without manipulative therapy in the management of back and/or neck pain in Danish children aged 9-15: a randomized controlled trial nested in a school-based cohort

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Title page

Title

Conservative care with or without manipulative therapy in the management of back and/or neck pain in Danish children aged 9-15: a randomized controlled trial nested in a school-based cohort

Short title: Manipulative therapy and children

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Abstract

Background

A substantial number of children experience spinal pain, i.e. back and/or neck pain. Today, no 'gold standard' treatment for spinal pain in children exists, but manipulative therapy is increasingly being used in spite of a lack of evidence of its effectiveness. This study investigates the effectiveness of adding manipulative therapy to other conservative care for spinal pain in a school-based cohort of Danish children aged 9-15 years.

Methods and Findings.

The design was a two-arm pragmatic randomized controlled trial, nested in a longitudinal open cohort study in Danish public schools. Two hundred thirty eight children from 13 public schools were randomized individually from February 2012 to April 2014. A text message system and clinical examinations were used for data collection. Interventions included either 1) advice, exercises, and soft tissue treatment, or 2) advice, exercises, and soft tissue treatment *plus* manipulative therapy. The primary outcome was number of recurrences of spinal pain. Secondary outcomes were duration of spinal pain, change in pain intensity, and Global Perceived Effect.

We found no significant difference between groups in the primary outcome (control group median 1 (IQR 1-3) and intervention group 2 (IQR 0-4), p=0.07). Children in the group receiving manipulative therapy reported a higher Global Perceived Effect: OR 2.22, (95% CI 1.19-4.15). No adverse events were reported. Main limitations are the potential discrepancy between parental and child reporting and that the study population may not be comparable to a normal care-seeking population.

Conclusions

Adding manipulative therapy to other conservative care in school children with spinal pain did not result in fewer recurrent episodes. The choice of treatment – if any – for spinal pain in children therefore relies on personal preferences, and could include conservative care with and without manipulative therapy. Participants in this trial may differ from a normal care-seeking population.

Trial registration: ClinicalTrials NCT01504698

Key words: randomized controlled trial, children, adolescents, spinal pain, back pain, neck pain, manipulative therapy

Strengths and limitations

- The school-based design minimized social bias and provided equal access for all.
- The prospective open cohort design allowed for a long follow-up period.
- The SMS track system is very efficient in collecting frequent data over a long time.
- The SMS track reflects how often parents reported spinal pain on behalf of the child, but this may not reflect the experience of the child.
- The inclusion criteria of a Numerical Rating Scale score of 3 or more on the day of examination and pain for at least 3 days is probably below the normal pain intensity threshold for seeking treatment.

INTRODUCTION

Spinal pain is common in children and adolescents and prevalence rates reach adult levels already around the age of 18[1]. For most children, episodes are transient and inconsequential and therefore the area has been largely ignored in research. However, some children have frequent, recurrent and bothersome complaints[2-5], impacting their mental wellbeing[6] and with the potential to decrease the level of physical activity. Importantly, these problems seem to track into adulthood, i.e. the most affected adolescents grow up to be the most affected adults[7 8]. Therefore, proper management at an early stage is essential to improve lifetime trajectories of spinal pain.

Management of children's musculoskeletal disorders relies to a large extent on parents' values, preferences and experience, and due to absence of guidelines for the treatment of spinal pain in children, healthcare professionals have to rely on guidelines developed for adults[9].

Manipulative therapy (MT) is defined as joint manipulation and/or mobilization with the aim to restore compromised function of joints[10]. This type of therapy is increasingly being used in children[11-13] because it is generally recommended as a treatment option for adults with spinal pain[14-18], and is delivered by various health professions, both on its own and in combination with other types of therapy, such as advice, exercises, and soft tissue treatment[18]. One study recently demonstrated a small but statistically significant effect of adding SMT to exercise therapy[19] in adolescents with low back pain. However this is the only full scale randomized controlled trial (RCT) conducted to date to investigate the effect of SMT in children with any type of spinal pain[9 20].

The aim of this pragmatic randomized controlled trial was to determine the effectiveness of adding manipulative therapy to other conservative care (advice, exercises and soft tissue treatment) on the number of recurrences of spinal pain in children aged 9 to 15 years who were participating in a school-based open cohort study. Secondary outcomes included the short-term effect on duration of spinal pain episodes, pain intensity, and Global Perceived Effect.

METHOD

Study design

A pragmatic parallel observer-blinded RCT nested in a school-based open cohort.

Participants and setting

This study was nested in The Childhood Health, Activity and Motor Performance School Study (CHAMPS Study-DK)[21], which is a Danish longitudinal school-based open cohort study including approximately 1,400 children aged 9 to 15 years from 13 public schools. The CHAMPS Study-DK was an open cohort study hence children could enter or leave the cohort at any time during the study period. The children were followed weekly with text messages (SMS) to one of their parents inquiring, amongst other things, about any musculoskeletal pain the child might have had during the past week (Questions in Supplementary File 1). Data collection on musculoskeletal complaints for this RCT began in February 2012 and ended at the end of June 2014.

Eligibility determination

All children enrolled in the CHAMPS Study-DK were invited to participate in the RCT. The complete protocol for the RCT is described in detail elsewhere[22]. Briefly, when a parent answered positively on the SMS to the presence of spinal pain in their child, a member of a screening team (licensed chiropractors and physiotherapists) telephoned the parent and conducted a standardized interview about the complaint, in order to determine whether the child was eligible for inclusion in the RCT. Initial eligibility was based on: 1) the pain was spinal and still present at the time of the interview, 2) the parent had agreed, on behalf of the child, to join the RCT, and 3) the child had not had any manual treatment of the spine during the previous 2 months. Within 2 weeks, the child was evaluated at the school by a chiropractor from the RCT team (seven licensed chiropractors) to determine whether he or she fulfilled the inclusion criteria (Table 1).

Table 1 Inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
• Pain in neck or back equal to or greater than 3 on an 11-box numerical rating scale for more than three days indicated by the child at the first visit	• Serious pathology (cancer, inflammatory diseases, vertebral fractures, cauda equina syndrome)
	• Manual treatment for the past 2 months (for this particular complaint)
	• Handicaps preventing normal physical activity

After the evaluation, both the child and his/her parents were informed about the results and treatment was initiated. The flow from SMS to RCT can be seen Figure 1.

Randomization

A computer-generated block randomization was made with block sizes alternating

between two and six at the time of inclusion, using a 1:1 allocation to the two groups. The consecutive designations of the two groups were written on separate pieces of paper and given to the chiropractors in the RCT team in sealed opaque envelopes. A research assistant, who was not otherwise connected to the study, performed the procedure.

First consultation

At the first consultation, the chiropractor obtained a case history, including pain intensity on an 11-box Numerical Rating Scale [23], performed a clinical examination, and various baseline data were acquired (Supplementary File 2). Two weeks after inclusion, the child was asked about Global Perceived Effect (Supplementary File 3) and pain intensity.

If a child experienced a recurrence of pain (i.e. the parent reported pain on the weekly SMS), the procedure was repeated except for randomization, which was carried forward throughout the study period regardless of the body location in which the complaint occurred. All data were filed in electronic data storage systems established specifically for this project and stored on secure servers.

Interventions

The non-manipulative therapy group (non-MT group) received advice, exercises and, soft tissue treatment, and the manipulative therapy group (MT group) received advice, exercises and, soft tissue treatment *plus* manipulative therapy (Table 2).

Table 2 Intervention groups

The non-manipulative group	The manipulative group received
• Pragmatic advice (activity level, ergonomics, cold packs etc.)	• Advice, exercises and soft tissue treatment

• Exercises (stretching and/or strengthening exercises) • Soft tissue treatment (manual trigger point therapy or massage)	• Manipulative therapy: joint manipulation and/or mobilization

Both groups were treated by the RCT team consisting of seven chiropractors. Manipulative therapy was defined as high velocity, low amplitude manipulation and/or mobilization of the joints to restore segmental spinal motion[10]. This was delivered at the discretion of the chiropractor and applied on the basis of a combination of biomechanical dysfunction and pain provocation responses found during the clinical examination of the child[10], since palpatory findings by itself have been found unreliable[24]. If the child experienced any pain in the extremities during the study period, these were also treated with manipulative therapy at the discretion of the treating chiropractor. Because of the pragmatic nature of the study, the frequency and content of treatments in both groups was determined by the treating chiropractor at each visit, similar to what is normal in clinical practice. Because the RCT team consisted of seven chiropractors, a child could be treated by different chiropractors during different appointments. Treatments continued until the child no longer had any symptoms related to the musculoskeletal complaint, or until the chiropractor or parent decided that further treatment was not indicated. The child and/or parents could terminate the treatments or drop out of the RCT at any time during the study period, but still stay in the cohort of the CHAMPS Study-DK.

Blinding

Due to the nature of the intervention, blinding of the treating chiropractors was not possible, however, neither parents nor children were informed about group allocation

and parents did not attend treatment sessions and answered the SMS without contact with clinicians or researchers. The coding of the intervention group was not revealed to the primary investigator or the statisticians until after the analyses had been completed.

Outcomes

The primary outcome was the number of recurrences as measured via the weekly SMS messages. A recurrence was defined as a new episode of spinal pain (i.e. back and/or neck pain) occurring after at least 1 week without spinal pain following the end of the previous episode. (See secondary outcomes, Table 3).

Table 3 Outcomes, definitions and statistical methods

Primary outcome	**Definition**	**Statistical method**
Number of recurrences of spinal pain (3-27 months follow up)	i) A positive answer on the weekly SMS for spinal pain ii) Minimum of 1 week without report of spinal pain prior to the recurrence	A hierarchical negative binomial regression model was used. Intervention effects were expressed as incidence rate ratio
Secondary outcomes		
Average duration of spinal pain episodes	The number of consecutive weeks the child was affected by spinal pain (response option '1')	A mixed effects linear regression model with subject as random effect, outcome log transformed was used. Intervention effects were expressed as the difference in median length
Total duration of complaint time in relation to individual follow-up time	Total number of weeks a child was affected by spinal pain (response option '1') in the entire follow-up period	A hierarchical negative binomial regression model was used. Intervention effects were expressed as incidence rate ratio
Global Perceived Effect after 2 weeks	Dichotomized into two groups: "Much better" and "The same or worse"	A logistic regression model was used. Intervention effects were expressed as odds ratios
Change in pain intensity after 2 weeks	Rated on an 11-point Numerical Rating Scale with	A linear regression model was used.

	'0' being 'no pain' and '10' being 'worst pain'	Intervention effects were expressed as the difference in mean length

Sample size

As the study had continuous inclusion, we continued to recruit participants until 3 months prior to the end of data collection in summer 2014, to include as many participants as possible with varying follow-up times. Based on preliminary analyses, this resulted in a power of 76% for the number of recurrences, 20% for episode length and 87% for overall complaint time[22].

Statistical methods

All analyses used an intention-to-treat approach. Various types of regression analyses were used depending on the type of outcome; follow-up time was included as an exposure time variable; subject was included as random effect in models with repeated measurements; and class and school were evaluated and included in the models as random effects if their effect was statistically significant (see details, Table 3). No effect was seen on any of the outcomes and hence, cluster was not included in the models. For linear models, means and standard deviations (SD) were used if data were normally distributed; otherwise medians and interquartile ranges (IQR) were reported. All methods were checked according to fulfilment of other assumptions and changed where appropriate. Due to some missing SMS answers, we imputed missing data as follows: if four or fewer consecutive missing answers were preceded and followed by a '1', this was considered as one continuous episode and the missing values were imputed as ´1'[3]. Since this type of outcome measure has not been used in previous trials, there is no consensus on how to substitute data. In a previous article we have described the

consequences of different data substitution strategies[3].

A sensitivity analysis was conducted to assess the effect of the choice of definitions in relation to recurrence and duration in the present study. In this analysis, a new episode was defined to occur after 4 weeks of 'no pain' instead of 1 week before it was considered a new episode.

STATA 14.2 (StataCorp, College Station, Texas, USA) was used for data analyses. Significance level was set to 5%.

Ethics

All parents gave written informed consent to participation on behalf of the child and the children gave oral consent. A child could be withdrawn from the study at any time during the study period and the study was conducted according to the Declaration of Helsinki. The project was approved by The Regional Committee on Health Research Ethics (#S-20110042) and data were handled according to the regulations set by the Danish Data Protection Agency (#2013-41-1738).

Patient and Public Involvement

There was no patient involvement in the formulation of the research question, the choice of outcome measures, the design, the recruitment procedures, conduct of the study or assessment of the burden of the intervention.

Parents of the included children will receive information about the study and its results via newsletters and the project's website.

RESULTS

The inclusion period ran from February 1st 2012 to April 1st 2014, and the follow-up period ended on June 27th 2014 (the end of the school year). Follow-up time was defined as "Number of days between inclusion date and last SMS". Since one child left the study the day after inclusion, this resulted in 1 to 868 follow-up days, (mean 477 days; SD 233). A total of 770 children reported spinal pain on SMS, and after telephone interviews, 483 children were evaluated for eligibility but did not fulfil the inclusion criteria. Additionally, 44 individuals reported pain less than 3 on the Numerical Rating Scale on the day of examination, leaving 243 children randomized and enrolled in the study. During data cleaning, we found five participants had been wrongly included, i.e. the SMS answer indicated no spinal pain, and they were excluded from the analyses. Thus, the final cohort for analysis consisted of 238 children with a mean age of 12.6 years: 116 in the non-MT group (49%) and 122 in the MT group (51%), (CONSORT Flow Diagram Fig 2).

Baseline covariates can be seen in Table 4, which also reports the amount of missing data for each variable. There was no difference between the groups for any of the covariates indicating randomization was successful and therefore univariate analyses were performed for all analyses.

Table 4 Baseline data. Baseline covariates by intervention group

	Non-MT group (n=116)	MT group (n=122)	Missing non-MT group*	Missing MT group*
Sex, Female, No (%)	73 (63)	78 (64)		
	Mean (CI)	Mean (CI)		
Age at inclusion	12.6 (12.4-12.9)	12.6 (12.3-12.9)		
Follow up time (days)	492 (448-536)	463 (423-504)		
Pain intensity at baseline (NRS)	5.3 (5.1-5.6)	5.2 (4.9-5.5)		

	Proportion (CI)	Proportion (CI)		
Expectations of the clinical course ("Worse")	7.6% (3.4-16.1)	7.6% (3.4-16.1)	32% (37)	35% (43)
	Median (IQR)	Median (IQR)		
KID Physical wellbeing	44.7 (38.5-49.6)	43.8 (40.5-49.6)	4% (5)	1% (1)
KID Psychological wellbeing	49.5 (44.8-56.0)	48.5 (44.8-56.0)	5% (6)	2% (3)
KID Autonomy and relation	49.5 (45.2-55.8)	49.5 (45.2-55.8)	4% (5)	2% (3)
KID Social support and peers	53.2 (46.9-57.8)	53.2 (46.9-57.8)	4% (5)	1% (1)
KID School	51.1 (45.4-58.2)	51.1 (45.4-54.4)	4% (5)	1% (1)

* Number of children with missing data according to intervention group; Non-MT: non-manipulative therapy; MT: manipulative therapy; CI: confidence intervals; NRS: Numerical Rating Scale; IQR: interquartile range; KID: KIDScreen domains

Primary outcome

During the follow-up period, 175 (74%) of the children had a total of 592 recurrences, ranging from 1 to 21 recurrences per child. The median number of recurrences was 2 (IQR 0-4) for the manipulative therapy group and 1 (IQR 1-3) for the non-manipulative therapy group, revealing no statistically significant difference between groups, incidence rate ratio (IRR) 1.26 (95% CI 0.98-1.61), p=0.07.

Secondary outcomes

We found no significant difference in the average episode length, total number of pain weeks or change in pain intensity between the two groups. Children in the group receiving manipulative therapy reported a higher Global Perceived Effect: odds ratio (OR) 2.22, (95% CI 1.19-4.15), that was statistically significant. All results are displayed in Table 5.

Table 5 Results on secondary outcomes

	MT group	**Non-MT group**
Length of spinal pain episode		
Total number of episodes	456 (55%)	374 (45%)
Median (IQR) (number of weeks)	2 (1-6)	2 (1-5)

β-coefficient (95% CI)	0.11 (-0.07; 0.29)	
P value	0.21	
Total duration of complaint time per child		
Total number of pain weeks	1-114	1-111
Median (IQR)	9 (IQR 4-22)	7 (IQR 4-18)
IRR (95 % CI)	1.16 (0.92-1.48)	
P value	0.22	
Global Perceived Effect		
Number of children in analysis*	96 (52%)	86 (48%)
OR (95% CI)	2.22 (1.19-4.15)	
P value	0.01	
NRS change		
Number of children in analysis*	112 (50%)	111 (50%)
Mean (SD)	2.2 (2.5)	2.3 (2.7)
β-coefficient (95% CI)	0.10 (-0.57; 0.78)	
P value	0.76	

* Number of children in analysis of the first episode due to missing data; IQR: interquartile range; IRR: incidence rate ratio; OR: odds ratio; NRS: Numerical rating Scale; SD: standard deviation

Sensitivity analysis on number of pain free weeks

The number of recurrences declined from a total of 592 to 259 when we defined a new episode to occur after 4 weeks of 'no pain' instead of 1 week. This, however, did not change the between-group difference on either the primary outcome or most of the secondary outcomes, but it did result in a statistically significant increased length of episode for the MT group, mean 3.5 (3.0-4.0) vs. 4.4 weeks (3.8-5.0) and median 2 (1-5) vs. 2 (1-4), P=0.045.

Harms

Adverse events can be defined as the sequelae following manipulative therapy to the spine that are medium to long term in duration, with moderate to severe symptoms, and of a nature that is serious, distressing and unacceptable to the patient and requires further treatment[25] To our knowledge, no adverse events following manipulative

therapy have been reported in children of this age group[26 27]. However, it is common to experience transient side effects such as temporary reddening or soreness in the area being treated after both soft tissue treatment and manipulative therapy[28]. Treating chiropractors recorded transient side effects if the child stated these at the consultation, but none were reported and no child was referred to other health care providers, including general practitioners, because of adverse events.

DISCUSSION

Adding manipulative therapy to other conservative care for children reporting spinal pain did not result in fewer recurrences in a school-based cohort of Danish children aged 9-15 years. Furthermore, the average episode length, total number of pain weeks, and change in pain intensity were no different between the groups. However, in the sensitivity analyses, filtering out the frequently recurring episodes, the difference for episode length did become statistically significant. Children randomized to the MT group reported a higher Global Perceived Effect that was statistically significant. Thus, no increased effectiveness was evident and no harm was detected.

To our knowledge, this is the first RCT evaluating the added benefit of manipulative therapy in children with spinal pain (i.e. back and/or neck pain). Michaleff et al[29] found only four RCTs dealing with conservative interventions for low back pain in children and all had a high risk of bias. Only one of these included manual therapy combined with exercise, but it had only 45 participants.

Because this study was a two-armed parallel trial with manipulative therapy as an

addition to other conservative care, it is probably not surprising that we did not find a large difference between the two groups. This RCT was nested in a large cohort study, and hence we could not prolong the study period to increase the sample size; however, given the small absolute differences found on both primary and secondary outcomes, this is unlikely to have changed our conclusions.

Choice of outcomes

We originally intended to analyze the three spinal regions separately, however the pain site could change within the same individual during follow up, and many individuals reported pain from several regions. Therefore, the interpretation of our results relate to 'spinal pain' as a coherent entity. We could not determine by the SMS answers whether recurrences were actual recurrences of the same problem at the same location in the spine, but simply conclude that there was subsequent spine-related pain. This can be considered a weakness as we cannot determine true recurrences; however it can also be considered to be a strength because pain in this age group appears to demonstrate a shift between regions of the spine over time, indicating that there is not independence between pain in the three regions[2]

The Numerical Rating Scale has been shown to be a valid tool for assessing pain in children[23 30 31], and in this study, the children also appeared to be able to rate their pain on the scale quite easily. However, when analyzing the data, we found that Numerical Rating Scale ratings were not always in accordance with Global Perceived Effect ratings, i.e. some children would say they felt better, although reporting a higher score on the Numerical Rating Scale at follow up than at baseline. This noise may be caused by variation in cognitive abilities and maturity between the children, and is probably

equally distributed between groups. Regardless, we did not find statistically significant differences between the groups on change in Numerical Rating Scale scores, and both achieved a mean change of 2.3, which can be regarded as a clinically meaningful change, as studies have shown a minimal clinically important change to be +/- 1[32 33].

We could not find any literature supporting the validity of measures of Global Perceived Effect in children, but validity of this measure has been shown to be good in adults[34 35] and we therefore included it as a measure of the child's own perception of improvement. We would have expected that statistically significant differences between the groups would follow the same pattern for the Numerical Rating Scale and the Global Perceived Effect, but this was not the case. Therefore, the validity of both of these as outcome measures in clinical trials involving children should be further explored.

Strengths and weaknesses

The principal strength of this study was the school-based design, which had a number of advantages: the logistical burden for the parents was reduced because the treatment took place during school time, social bias was likely to be minimal or absent because everybody was invited to participate in the study, and there was equal access because all treatment in the trial was free. Also, this design allowed for a long follow-up period for most children. By nesting this RCT in a school-based cohort, we may however have included children who would not normally have sought care, i.e. likely to have had sub-clinical pain. The inclusion criterion of a Numerical Rating Scale score of 3 or more on the day of examination is probably also below the normal pain intensity threshold for seeking treatment and many parents would probably have waited until the pain had

become worse or lasted longer before seeking care. On the other hand, the number and duration of spinal pain episodes were higher in the study sample than in the full cohort (mean number 3.5 versus 2, mean duration 4.6 versus 2.8)[36], suggesting that the children enrolled in this study were more affected by pain than their non-participating peers.

SMS is a very efficient way of collecting frequent data over a long time[37 38]. In this study, the SMS responses were a reflection of how often the parents reported on their child's pain and might not have been a true reflection of how the child actually felt. We know that there is a discrepancy between parent and child reporting of spinal pain[39-41]. Parents appear to under-report compared to their child when pain is at a low level, whereas concordance is higher when the pain is more severe. Thus, it is possible that the parents stopped reporting pain because they assumed the complaint to be minor, even though the child might still have had pain. This could explain some of the difference between outcomes reported by the children (Global Perceived Effect) and outcome reported by the parents (SMS).

Using different practitioners prevents a potential patient-practitioner relationship and is considered a strength; however, the more people involved, the more irregularities and mistakes are likely to occur. One example of this is the poor response rate to the measures collected by the clinicians, e.g. Numerical Rating Scale and Global Perceived Effect scores.

Missing data

The amount of missing data was substantial for some of the secondary outcomes, and therefore we analyzed only those for the first spinal pain episode. However, there was no difference in response rates between groups, and it was assumed that data were missing completely at random and not due to any underlying confounding factors or bias. Possible reasons for missing data could be practitioners' forgetfulness or an electronic system defect resulting in missing data. Because of missing data, we cannot say anything valid about the course of pain, e.g. whether there is a learning effect over time or whether expectations of treatment differ over time between the two groups.

Future research

Since the inclusion criteria in this study were very broad, subgroup analyses would be valuable to inform future studies, i.e. if there are subgroups of children who respond better or worse to manipulative therapy than to other treatments. Future RCTs should include care-seeking children who self-report their response to treatment in order to evaluate effectiveness in that population. In addition, inclusion of an untreated group would elucidate the effect of treating these children, whether manipulative therapy is included or not.

Conclusion

We found no significant difference in the number of recurrences of episodes of spinal pain in a school-based cohort of children when adding manipulative therapy to advice, exercises, and soft tissue therapy. The study population may not be comparable to a normal care-seeking population and therefore the results may not be directly transferrable.

Authors' contributions

All authors (KBD, JH, NW, LH) participated in the design and interpretation of analyses of this study. Kristina Boe Dissing was project manager for the trial and drafted the manuscript. All authors (KBD, JH, NW, LH) contributed with revisions and approved the final version of the manuscript.

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Competing interests

The authors have no competing interests to declare.

Data sharing statement

Data are from the Childhood Health, Activity and Motor Performance School Study (CHAMPS Study-DK) and are available on request from the project manager Niels Wedderkopp

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Figure legends

Figure 1 Flow from SMS to RCT.

RCT: randomised controlled trial. SMS: text message. MT group: manipulative therapy group. Non-MT group: non-manipulative therapy group

Figure 2 CONSORT Flow Diagram

Supporting information

Supplementary File 1. SMS questions

Supplementary File 2. Covariates, baseline data and definitions

Supplementary File 3. Global perceived effect question

CONSORT checklist

Study protocol

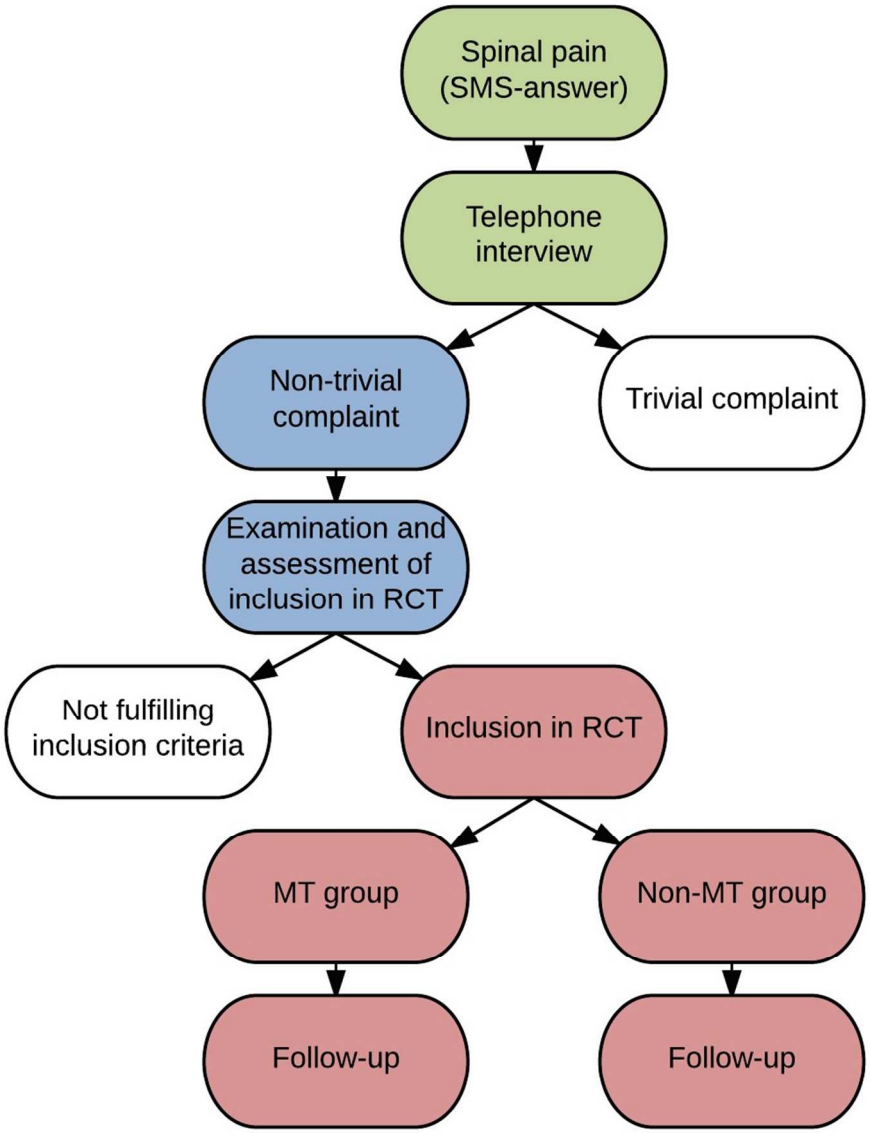

Figure 1 Flow from SMS to RCT

85x115mm (300 x 300 DPI)

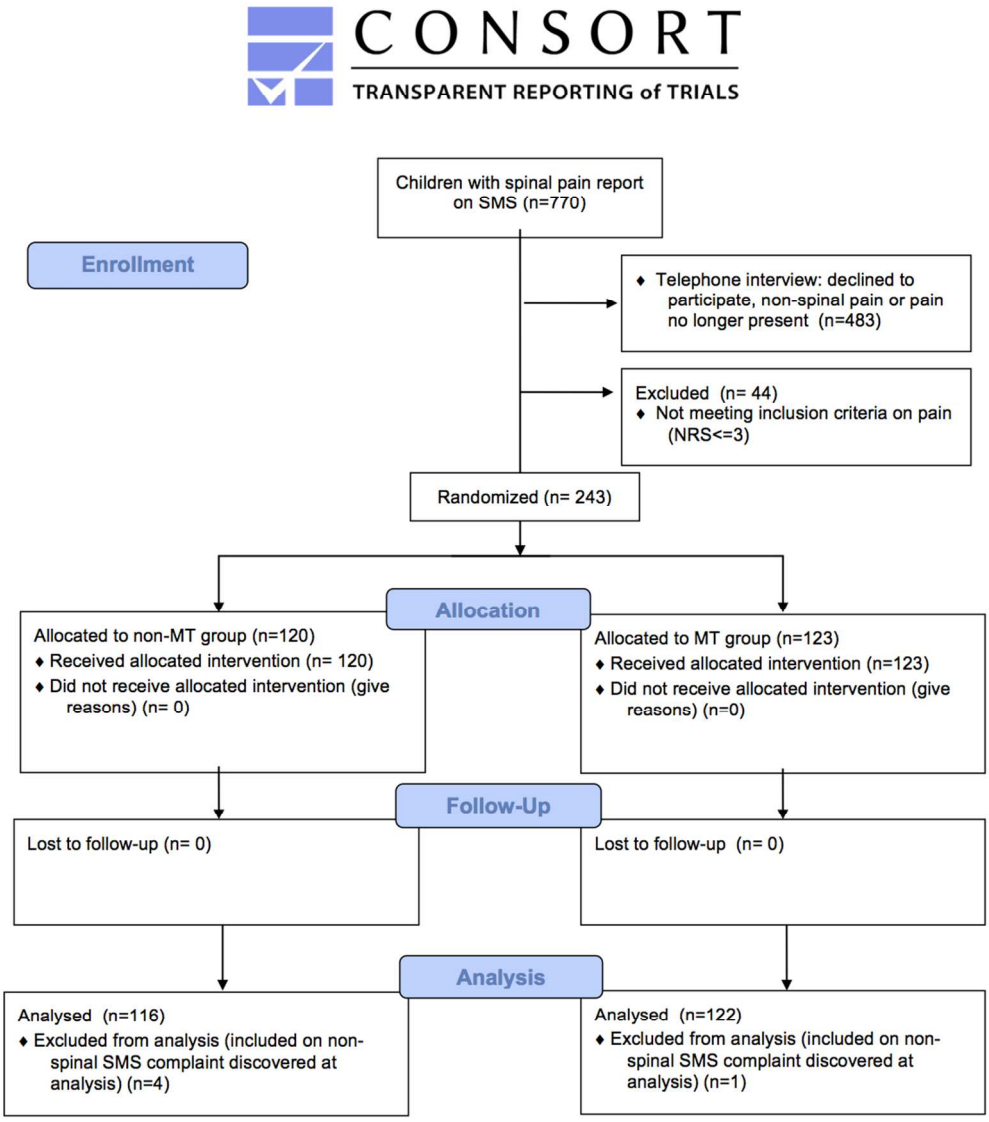

Figure 2 CONSORT Flow Diagram

97x110mm (300 x 300 DPI)

Supplementary File 1

SMS questions

1. **Has <FIRSTNAME> had pain for the last week?**

1.Neck, back or lumbar spine
2.Shoulder, arm or hand
3.Hip, leg or foot
4.No, my child has not had any pain

2. **How many times has <FIRSTNAME> been to organized sports in his/her leisure time in the past week?**

0 = 0 times
1 = 1
2 = 2
3 = 3
4 = 4
5 = 5
6 = 6
7 = 7
8 = more than 7 times

3. **<FIRSTNAME> which kinds of sports?**

1 Soccer
2 Handball
3 Basketball
4 Volleyball
5 Gymnastics
6 Tumbling
7 Swimming
8 Horse back riding
9 Dancing
10 Other

Supplementary File 2. Covariates, baseline data and definitions

Covariates	**Definitions**
KIDSCREEN 27 questionnaire	Quality of life measured from 27 questions covering the following five domains. Values vary from 10-70 with population norm mean=50, high value equals better QOL
KID Physical	Physical wellbeing domain
KID Psych	Psychological wellbeing domain
KID Autonomy	Autonomy and parent relation domain
KID Social	Social support and peers domain
KID School	School domain
Expectations of the clinical course (EoCC)	The child was asked before the treatment: "What do you expect the outcome of your spinal pain will be compared with how it is now?" Rated on a 5-point scale ('1' being 'much worse' and '5' being 'much better')
Baseline data	
Age	9-15 years
Sex	Boy/girl
Intervention group	Manipulative group/non-manipulative group
School	13 schools included (used as cluster)
Class	4th to 9th grade (used as cluster)

Supplementary File 3

Global perceived effect

Name:
Id number:

Date:

How will you describe your general wellbeing now in your neck/back (and any extremities) as opposed to 2 weeks ago before treatment was started?

(Only one tick in the following)

- Much better
- Better
- Little better
- Almost the same
- Little worse
- Worse
- Much worse

Rated in the file from 1-7, with 1 being much better and 7 being much worse.

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)	3
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	5
	2b	Specific objectives or hypotheses	5
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	6
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	
Participants	4a	Eligibility criteria for participants	6-7
	4b	Settings and locations where the data were collected	6
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	8-9
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	9-10
	6b	Any changes to trial outcomes after the trial commenced, with reasons	16
Sample size	7a	How sample size was determined	10
	7b	When applicable, explanation of any interim analyses and stopping guidelines	
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	7
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	7
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	7
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	7
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those	9

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

*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.