PROTOCOL TITLE:

Myofascial and Articular Treatment of Adolescent Idiopathic Scoliosis

Preliminary Feasibility Study

PRINCIPAL INVESTIGATOR:

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REGULATORY FRAMEWORK:

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FUNDING:

Not yet funded

CLINICAL TRIALS

Is this a clinical trial per the NIH definition of a Clinical Trial? X Yes ☐ No

NIH Definition of a Clinical Trial:

A research study in which one or more human subjects are prospectively assigned to one or more interventions. An "intervention" is defined as a manipulation of the subject or subject's environment for the purpose of modifying one or more health-related biomedical or behavioral processes and/or endpoints. Examples include: drugs/small molecules/compounds; biologics; devices; procedures (e.g., surgical techniques); delivery systems (e.g., telemedicine, face-to-face interviews); strategies to change health-related behavior (e.g., diet, cognitive therapy, exercise, development of new habits); treatment strategies; prevention strategies; and,

diagnostic strategies (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes.

Use the following four questions to determine the difference between a clinical study and a clinical trial:

1) Does the study involve human participants? ☒ Yes ☐ No
2) Are the participants prospectively assigned to an intervention? ☒ Yes ☐ No
3) Is the study designed to evaluate the effect of the intervention on the participants? ☒ Yes ☐ No
4) Is the effect being evaluated a health-related biomedical or behavioral outcome? ☒ Yes ☐ No

Note that if the answers to the 4 questions are yes, your study meets the NIH definition of a clinical trial, even if…

- You are studying healthy participants
- Your study does not have a comparison group (e.g., placebo or control)
- Your study is only designed to assess the pharmacokinetics, safety, and/or maximum tolerated dose of an investigational drug
- Your study is utilizing a behavioral intervention

If yes to all 4 questions, please confirm that the research team is familiar with and agrees to comply with the investigator requirement to register the study on the ClinicalTrials.gov database. Additionally, the approved consent document(s) must be uploaded to the ClinicalTrials.gov database ☒ Yes ☐ No

For any assistance with registration of your trial or the requirements, please contact HSC-CTSCResearchConcierge@salud.unm.edu

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1. Objectives

1.1 Study Purpose

The purpose of this study is to conduct a pilot study of the Dynamic Myofascial and Articular Mobilization and Reorganization (DMAMR) treatment in Adolescent Idiopathic Scoliosis (AIS). We propose the implementation of Dynamic Myofascial and Articular Mobilization and Reorganization (DMAMR) protocol can (a) decrease and/or reduce progression of spinal curvatures, (b) reduce degree of anatomical rib hump deformity common in AIS, (c) decrease incidence of patients requiring corrective bracing and/or corrective spinal surgery, (d) significantly reduce AIS-associated pain, and (e) improve quality of life for AIS patients.

Specific Aims

As a preliminary feasibility study, there are specific aims that we will address:

1. Sufficient subjects will be willing to participate in this study (Recruitment and Consent).
2. Sufficient subjects in the active treatment group will be willing to undergo treatment for the 6 months (Dropout rate will be low enough or late enough to avoid undermining statistical analysis).
3. Sufficient subjects in the active treatment group will perform independent exercise, use arch supports as necessary, heel lifts, ischial lifts, as prescribed (Compliance).
4. Quality of data will be sufficient to provide the basis for the desired statistical analysis (Collection and Data Entry).

5) Furthermore, if this research project goes well with regard to the elements 1-4 stated above, we may have enough data to assess other aspects of the impact of this treatment protocol. Ordinarily it would be thought that we would have to follow the treated subjects through until skeletal maturity to assess the impact of a prior intervention on the requirement for bracing or spinal surgery. There may be a difference between the treatment group and the control group in the number of those subjects who were not braced, but who then require bracing at the end of the 6 month intervention period. Likewise, there may be a difference between the treatment group and the control group in terms of how many require surgery at the end of the 6 month intervention period. Also, while we cannot predict the curve progression of any single child or adolescent, we do have aggregate statistics about likely progression of curvatures for subjects of particular ages and particular degrees of curvature. For this reason, studies that involve AIS interventions that take place over 6-month periods of time may produce statistically significant changes in the likelihood of requiring bracing or surgery (references 3,4,5). The biostatistician has confirmed that we may well have the number of subjects and

the study design that could shed important light on the ultimate goals of a long term research strategy, the hypotheses of which are stated below.

1.2 Hypotheses

This study will test whether DMAMR produces clinically relevant changes in progression of scoliosis curvatures and rib humps**,** and whether this treatment protocol improves pain scores and quality of life.

Current research has demonstrated unilateral muscle shortening in AIS. Of most importance for this research proposal, research has also identified a set of muscles, portions of which are at an angle to the spine, that are shorter on the concave side of the curvature: the quadratus lumborum, psoas major and minor, and the abdominal obliques. The researchers have suggested this is a compensatory effect of the spinal deformities seen[1]. We agree that unilateral muscle shortening is present in AIS but we suggest that this asymmetry represents differences between muscle tension on either side of the spine and results in a tethering effect on the spine itself. Supporting a finding of the importance of these muscle imbalances, research using individualized physical therapeutic exercise programs to balance these types of muscle imbalances has demonstrated effectiveness in AIS treatment[2] [3] [4] [5].

We hypothesize this asymmetrical muscle imbalance, and its resultant tethering effect on the spine, represent myofascial dysfunction. We believe the forces generated by this dysfunction are sufficient to induce worsening of the AIS curvature. The myofascial factors involved in the tethering of the spine in AIS include asymmetrical muscle imbalances involving muscles at an angle to the spine, primarily iliopsoas, quadratus lumborum, abdominal obliques, latissimus dorsi, and anterior serratus muscles.

Fascia overlies and interpenetrates these muscles. At a critical point, these myofascial imbalances generate sufficient stress on the overlying fascia to create a further contractile force within the fascia itself. We ask whether this contractile force is mediated not only by

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[1] Fadzan M, Bettany-Saltikov J. Etiological Theories of Adolescent Idiopathic Scoliosis: Past andPresent. Open Prthop J. 2017; 11:1466-1489.

[2]Fusco C, Donzelli S, Lusini M, et al. Low rate of surgery in juvenile idiopathic scoliosis treated with a complete and tailored conservative approach: end-growth results from a retrospective cohort. 2014 Scoliosis 9 (12), 2-6.

[3] Negrini S, Atanasio S, et al. Effectiveness of complete conservative treatment for adolescent idiopathic scoliosis (bracing and exercises) based on SOSORT management criteria: results according to SRS criteria for bracing studies. 2009 Scoliosis 4(19), 1-12.

[4] Romano M, Negrini A, et al. SEAS (Scientific Exercises Approach to Scoliosis): a modern and effective evidence based approach to physiotherapeutic specific scoliosis exercises. 2015, Scoliosis 10 (3), 1-19.

[5] Schreiber S, Parent EC, Hill DL, et al. Schroth physiotherapeutic scoliosis-specific exercises for adolescent idiopathic scoliosis: how many patients require treatment to prevent one deterioration?-results from a randomized controlled trial- Scoliosis and Spinal Disorders (2017) 12:26.

anatomic shortening of individual muscle groups but also by intrinsic changes in fibroblast gene expression within the fascia itself [6].

We further hypothesize that the asymmetrical muscle imbalances observed in AIS may be part of a larger contracted fascial spiral force influencing the development and progression of deformity. Therefore, treatment of the muscles, fascia, and related articular dysfunction may contribute to the control or reduction of AIS-associated deformities including scoliotic curvatures and accompanying rib humps. Effective treatment of these imbalances and deformities may reduce or eliminate AIS-associated spinal area pain, which we hypothesize is largely myofascial in nature.

2. Background

2.1: Defining the problem and gaps in current knowledge.

The Scoliosis Research Society has defined scoliosis as a lateral curvature of the spine greater than 10° as measured using the Cobb method on standing radiograph [7]. Scoliosis is present in 2-4% of children between 10 and 16 years of age [8]. Curve progression in adulthood is related to the degree of curvature at skeletal maturity. Curves of less than 30° at maturity are unlikely to progress. Curves of 30-50° progress at an average of 10-15° over a lifetime. Curves greater than 50° at maturity progress steadily at a rate of 1° per year [9]. Curve progression in adulthood is a key factor in chronic pain and disability. Clinically significant rib cage distortion can result in respiratory insufficiency and cor pulmonale [10].

In the last 25 years, there have been significant advances in our understanding of the genetics and biochemistry correlated with scoliosis. Multiple studies have identified abnormalities of spinal bone tissue as well as genetic abnormalities involved in AIS [11] [12]. Unfortunately, no successful intervention strategies based on this new knowledge have been developed to date. The standard treatment over many decades has been using bracing to decrease progression of the curvature and avoid spinal surgery. This treatment has been shown to be effective for a significant portion of adolescents with scoliosis [13]. While there is continuing consensus that

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6 Chaitow L (Ed.), Facial Dysfunction: Manual Therapy Approaches. 2014: Handspring, Edinburgh, Scotland, UK.

[7] Kane WJ. Scoliosis prevalence: a call for a statement of terms. Clin Orthop. 1997; 126, 43-46.

[8] Roach JW. Adolescent idiopathic scoliosis. Orthop Clin North Am.1999; 30, 353-365.

[9] Miller NH. Cause and natural history of adolescent idiopathic scoliosis. Orthop Clin North Am. 1999. 30, 343-352.

[10] Barois A. Respiratory problems in severe scoliosis. Bull Acad Natl Med. 1999;183(4)721-30.

[11] Newton Ede MMP, Jones SW. Adolescent idiopathic scoliosis: evidence for intrinsic factors driving aetiology and progression. International Orthopaedics (SICOT) (2016) 40:2075-2080.

[12] Fadzan M, et al. 2017

[13] Negrini S, Minozzi S, et al. Braces for idiopathic scoliosis in adolescents. Cochrane Database Syst Rev 2015 Jun18;(6)CD006850.

scoliosis is a multifactorial disorder, there is little in our understanding of the contributing factors that currently inform interventions successful in altering its clinical course. Importantly, existing treatments are focused on slowing progression of curvature, because no treatments have been shown to actually reverse the condition.

The one notable recent addition to the therapeutic options is the emerging consensus that individualized exercise focusing on addressing muscle imbalances, and thereby decreasing asymmetrical loading of the spine, can improve the outcome of scoliosis care and reduce the need for corrective surgery [14] [15] [16] [17].
There is a continuing need to develop a comprehensive program that is both individualized and multifactorial. This research study and the proposed treatment protocol aim to demonstrate that – by utilizing a myofascial and articular approach to treatment – it is possible to successfully reduce the rate of progression of scoliosis and/or reduce the degree of curvature. Successful application of this conservative approach has the potential of reducing the need for corrective surgery.

2.2.: Relevant Preliminary Data:

It is worthwhile to consider the different biomechanical factors seen in the myofascial dysfunction we hypothesize to be mediating AIS. These factors inform a conservative and integrated myofascial approach to treatment.

Whyte Ferguson developed such a course of individualized multi-factorial treatment over the course of 15 years. This protocol was documented in the treatment of 22 individuals with defined or developing scoliosis detailed in the case series *Adolescent Idiopathic Scoliosis: The Tethered Spine III: Is Fascial Spiral the Key?* [18]. The treatment approach focused on addressing unbalanced fascial tension in the torso, and accompanying myofascial dysfunction and related myofascial pain, generally focused on muscles at an angle to the spine rather than the paraspinal muscles. Articular dysfunction related to these fascial and muscle imbalances was also addressed. Among the significant results of the treatment regimen developed were:

1. Case 1 with a 20° curvature at age 10 , who, after treatment, had an 8° curvature at age 11.
2. Case 10 who had a kyphoscoliosis of 63° at age 18 and a thoracolumbar scoliosis with a rib hump that was 15° on the first visit and was 8° on the second visit and 4° on the third visit, as measured by scoliometer. Over several months of care, his kyphoscoliosis was also reduced to 50°.
3. Case 9 with a 20° thoracolumbar curvature at age 14 years two months whose rib hump decreased in severity but the scoliotic curve increased to 30° while under

[14] Fusco et al., 2014.
[15] Negrini et al., 2009.
[16] Romano et al., 2015
[17] Schreiber et al., 2017
[18] Whyte Ferguson L. Adolescent idiopathic scoliosis: the tethered spine III: is fascial spiral the key? Journal of Bodywork and Movement Therapies 21 (2017)948-971.

treatment, but then the treatment approach was changed, and 5 more treatments were performed over the next 7 weeks. At this point, a new set of x-rays was performed at the regional orthopedic center and her curvature was reduced to 16° and the bracing that had been expected was avoided.

4. Case 2 with an 18° curvature at age 9 and 11° curvature 2-1/2 months later. After a decrease in frequency from care once every 2 weeks to only 6 treatments over the next 5 months, the curvature increased to 14°. The patient received only 3 treatments in the following 5 months and the curvature increased to 20°. The patient had no further care because her family moved out of state, but she reached bone maturity 4 years later with a curvature of 27°. She was not prescribed a brace during those four years because she had a negligible rib hump.

It is important to note that current understanding of AIS progression is that, once a rib hump develops, the anatomic curvature shifts from functional to structural. In the course of this extended case series and with the progression of the practitioner's advanced skills in addressing fascial imbalance, muscular imbalance, and related articular dysfunction, the time it took to reduce rib humps became shorter, and there was an increase in the degree of reduction of the rib humps. In the case series referred to above, 17 cases had significant rib humps at the beginning of their care and of these, 10 had reduction of their rib humps to the point that Adam's Forward Bend Test was negative for rib hump or the remaining rib hump was minimal. It is important to note that these improvements maintained over time. Because the DMAMR protocol was so successful, we must conclude that there is a considerable degree of plasticity of the rib cage in adolescents.

While promising, the above results are from case study data only. Only by performing systematic controlled research with observations and measurements performed by blinded individuals, can we assess the significance of the case study findings described above. There is a critical need for powerful conservative treatment approaches to address AIS and reduce the need for surgery. The DMAMR treatment protocol to be evaluated in this proposed research project may hold promise to achieve this goal. It is also hoped that this research project will demonstrate improvement in pain levels and quality of life.

2.3.: Significance of research based on existing literature; how the proposed research will add to existing knowledge:

In addition to the literature review that was part of the article published by Whyte Ferguson referenced above, there have been important additions to our understanding of AIS that add to the importance of the proposed research. These findings address the four biomechanical factors discussed below and further corroborate the need for a successful multifactorial and individualized treatment protocol:

1. ***Muscle Imbalances***

   To date, research on muscle imbalances has focused on the paraspinal muscles and it has been difficult to establish that there are any significant histological or muscle fiber activity differences between the muscles on the convex and concave sides of the spine.

Further, what differences were found could as easily be explained as the result of the curvature rather than contributing to its causation [19].

Importantly, recent genetic studies have provided evidence that skeletal muscle dysfunction could be a contributory factor in AIS susceptibility: rare variants in fibrillin-1 and fibrillin-2 have been found to be associated with severe AIS. These glycoproteins form key components of skeletal muscle myofibrillar structure and abnormality of fibrillin-1 is associated with the connective tissue disorder, Marfan's. Importantly, 60% of patients with Marfan's develop scoliosis [20]. Recent research reported signs of muscle myopathy and muscular atrophy on both the convex and concave sides of the scoliosis apex [21]. These findings accentuate the fact that muscle and associated soft tissue abnormalities are the norm in severe AIS, but these abnormalities still do not explain the dynamics of the development of the AIS.

In the AIS treatment protocol used in the case series cited above, the treatment of muscle imbalances was most effective when it focused on muscles at an angle to the spine. Research is beginning to address the importance of several of these muscles. Increased curvature in the lumbar spine is associated with longer appearance of the 12th rib on the ipsilateral side and there is no such correlation in normal controls. It is suggested by the authors that the greater activity of the Quadratus lumborum on the side of the lumbar convexity may account for the lower rib asymmetry, due to the fact that the Quadratus lumborum is the largest of the muscles that attach to the ribs, as well as to the spine and the ilium [22]. When researchers used Botulinum toxin A to temporarily paralyze the Psoas major in 9 adolescent subjects, radiographs taken 6 weeks later showed a significant decrease in both the lumbar and the thoracic spine Cobb's angles, with a non-significant decrease in both lumbar and thoracic derotation [23].

In the research proposed here, treatment will be focused on elongating muscles that are palpably shortened, including the Iliopsoas and the Quadratus lumborum. It is important to note that the potential importance of the Iliopsoas does include the fact

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[19] Mannion AF, Meier M, Grob D, et al. Paraspinal muscle fiber type alterations associated with scoliosis: an old problem revisited with new evidence. Eur Spine J 7::289-293, 1998.

[20] Buchan JG, Alvarado DM, Haller GE, et al. Rare variants in FBN1 and FBN2 are associated with severe adolescent idiopathic scoliosis. Mum Mol Genet 23:5271-5282, 2014.
[21] Wajchenberg M, Martins DE, Luciano RP, et al. Histochemical analysis of paraspinal rotator muscles from patients with adolescent idiopathic scoliosis: a coss-sectional study. Medicine (Baltimore) 2015. 94:e598.
[22] Grivas TB, Burwell RG, Kechagias V, et al. Idiopathic and normal lateral lumbar curves: muscle effects interpreted by 12th rib length asymmetry with pathomechanic implications for lumbar idiopathic scoliosis. Scoliosis and Spinal Disorders 2016. 11(suppl 2):35.
[23] Wong C, Gosvig K, Sonne-Holm S. The role of paravertebral muscles in adolescent idiopathic scoliosis evaluated by temporary paralysis. Scoliosis Spinal Disord. 2017 Oct 10;12:33.

that it attaches to each of the lumbar vertebrae, but from the lumbar spine the muscle angles laterally and inferiorly to the upper medial femur and this angulation may give it particular import in contributing to AIS curvatures. (Figure 1)

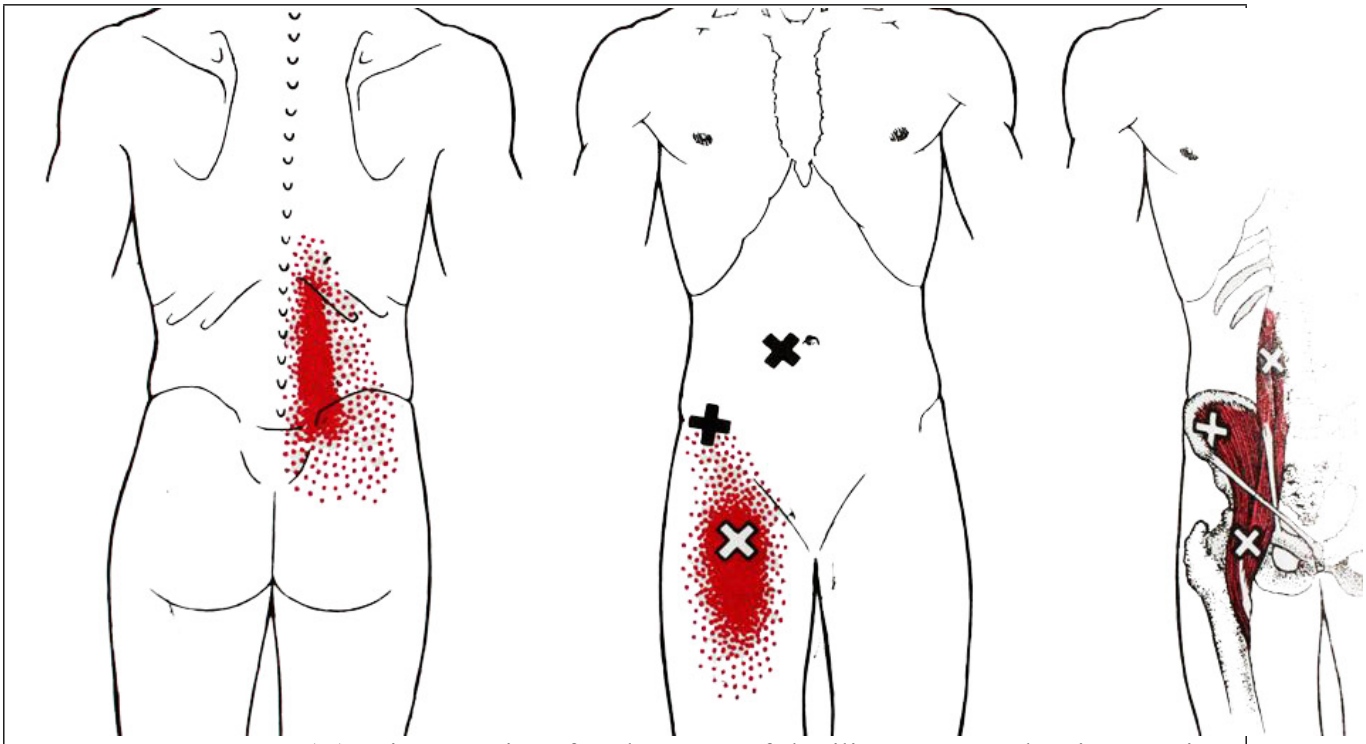


Figure 1. Iliopsoas. (A) Primary pain referral pattern of the iliopsoas muscle trigger points (TrPs). (B) Trigger point locations and secondary pain referral zone. (C) Anatomical rendering demonstrating psoas (superiorly), iliacus (middle) and common insertions at the lesser trochanter of the femur (inferiorly).

Source: Travell, J.G., Simons, D.G., 1992 Mofascial Pain and Dysfunction: The Trigger Point Manual. In: Lower Body. Vol.2. Williams & Wilkins, Baltimore.

Similarly, the Quadratus lumborum does attach to the lumbar spine and the ribs and ilium, but Whyte Ferguson found, in the case series study referenced above, that different portions of the Quadratus lumborum were shortened on the convex and concave sides of the lumbar curvature. The iliolumbar portion of the Quadratus lumborum was shorter on the side of convexity of the lumbar spine (in 19 out of 20 cases) thus potentially pulling the lumbar spine toward the left ilium. The iliocostal portion of the Quadratus was shorter on the side of concavity of the lumbar spine (in 19 out of 20 cases) thus potentially pulling the ilium and the rib cage closer to each other and contributing to the concavity of the lumbar curvature. (Figure 2) Pelvic obliquity may be a factor that disposes the iliolumbar portion of the Quadratus lumborum to shorten on the side that is less well supported by the pelvis

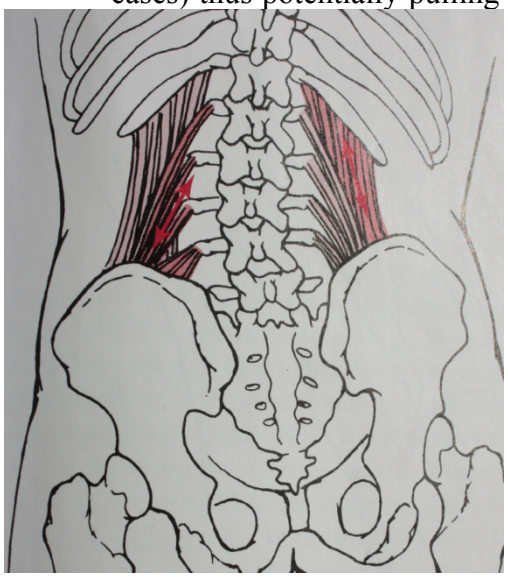


Figure 2. Quadratus lumborum. Left side highlights iliolumbar portion attached to the lumbar spine and contributing to the convexity of the lumbar curvature. Right side highlights iliocostal portion that approximates the ilium and the lower rib contributing to the concavity of the lumbar curvature.

Source: Travell, J.G., Simons, D.G., 1992 Mofascial Pain and Dysfunction: The Trigger Point Manual. In: Lower Body. Vol.2. Williams & Wilkins, Baltimore.

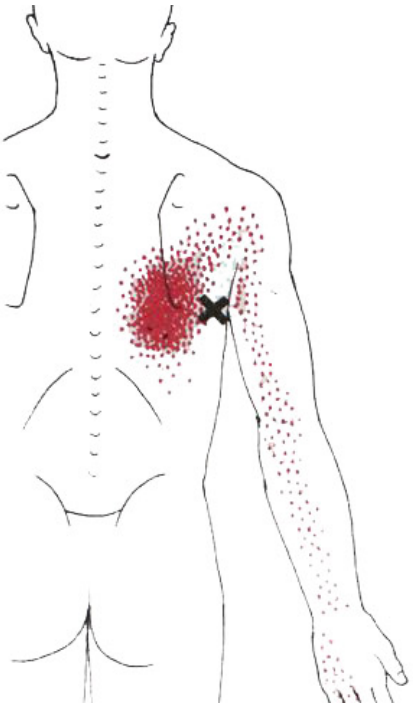
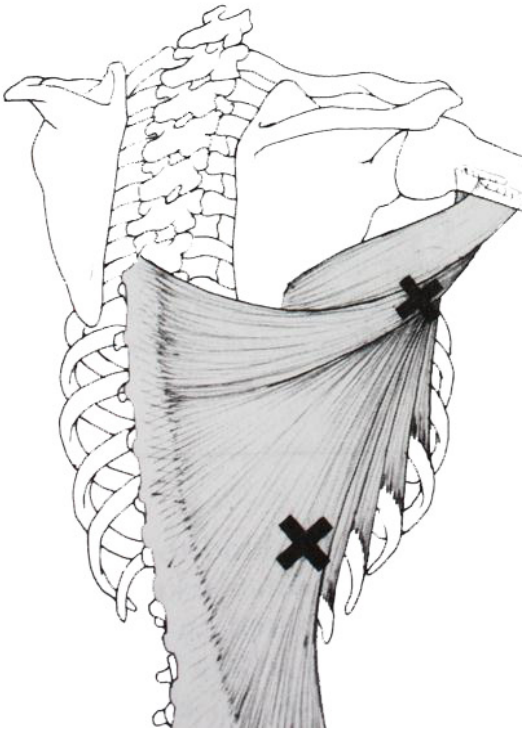


Figure 3. Latissimus Dorsi. (A) Primary pain pattern and superior TrP. (B) Anatomical rendering and superior and inferior TrPs.



Source: Simons, D.G., Travell, J.G., Simons, L.S. 1999 Mofascial Pain and Dysfunction: The Trigger Point Manual. In: Upper Half of Body. Second ed., Vol.1. Lippincott, Williams & Wilkins, Baltimore.

Whyte Ferguson also noted that the latissimus dorsi and anterior serratus were shortened in the thoracic spine region, on the side of the rib hump and appeared likely to contribute to the forces bending and deforming the ribs. (Figure 3 and 4)

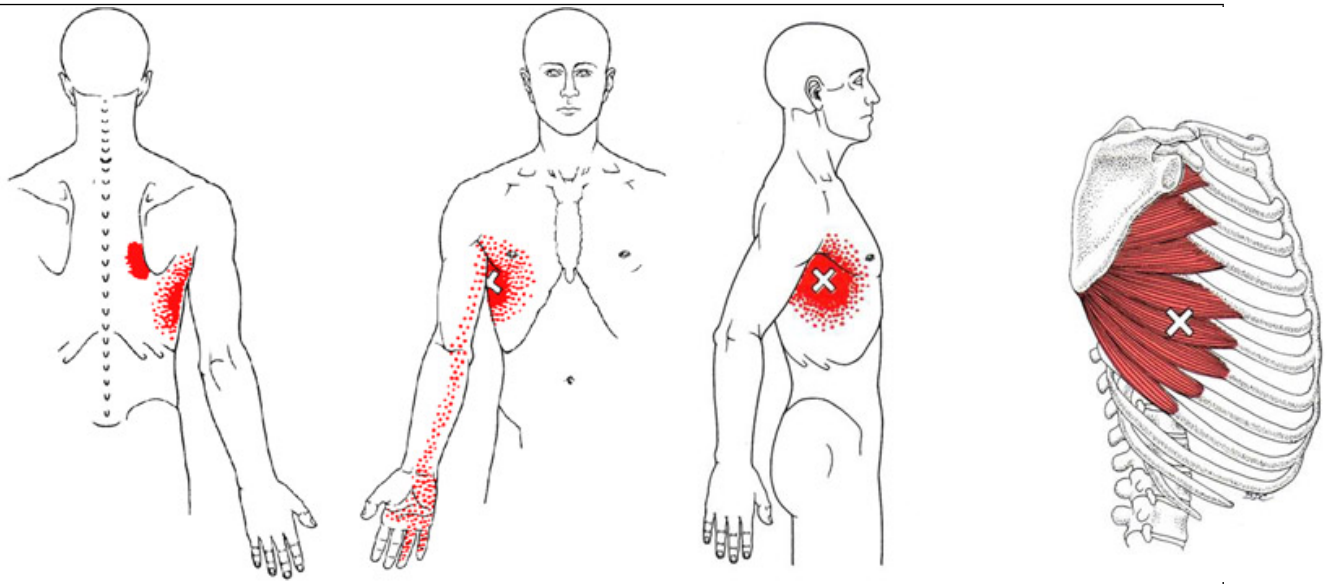


Figure 4. Anterior Serratus. (A, B, C) Pain referral zones and TrP in multiple anatomical planes (D) Anatomical rendering and TrP.

Source: Simons, D.G., Travell, J.G., Simons, L.S. 1999 Mofascial Pain and Dysfunction: The Trigger Point Manual. In: Upper Half of Body. Second ed., Vol.1. Lippincott, Williams & Wilkins, Baltimore.

The AIS treatment protocol in the proposed research project will include using myofascial release techniques to address muscle asymmetries and balance muscle tensions around the spinal curvatures, focusing especially on the muscles that are at an angle to the spine. Exercises including stretching will also be prescribed to release muscles that are tighter on one side of the spine than the other, and to strengthen muscles that are weaker on one side of the spine than the other.

2. ***Pelvic Obliquity***

Whyte Ferguson's AIS treatment protocol also focuses on balancing the pelvis to reduce pelvic obliquity and address leg length inequality, and unbalanced height of the ilia when seated. Research has corroborated the association of sacral slanting with pelvic obliquity and lumbar curvature in AIS and there is also some correlation between leg length difference and sacral slanting [24]. Pelvic rotation has been found to correlate with rotational status of both the lumbar spine and thoracic spine [25].

Most of the literature supposes that the pelvic imbalances are a compensation for the curvatures of the spine. But it could easily be the case that the sacrum provides the base that the spine sits on and if the sacrum is lower on one side, or is rotated posterior to the plane of the spine and therefore does not as successfully support the spine, the lumbar spine may tend to deviate to the less supported side. In the proposed research, the unbalanced hip height while standing may be addressed with a heel lift for the patient to wear in footwear. The unbalanced hip height while seated will be addressed with an ischial lift, an approximately 3/8" thick magazine, for the subject to sit upon whenever seated for extended periods of time. Heel lifts and ischial lifts will be provided to the subjects in this study as appropriate. The pelvic obliquity will be addressed by both gentle chiropractic manipulation of the sacroiliac joints and osteopathic mobilization of the ilium or ilia and the sacrum.

Since addressing the pelvic obliquity and unbalanced hip height were found to be very important in the treatment protocol of the case series cited above, we may be able to learn whether the imbalances of the pelvis are compensatory to the spinal curvatures, or whether rather the imbalance of the pelvis may be a factor contributing to progression of AIS.

3. ***Ligamentous Laxity***

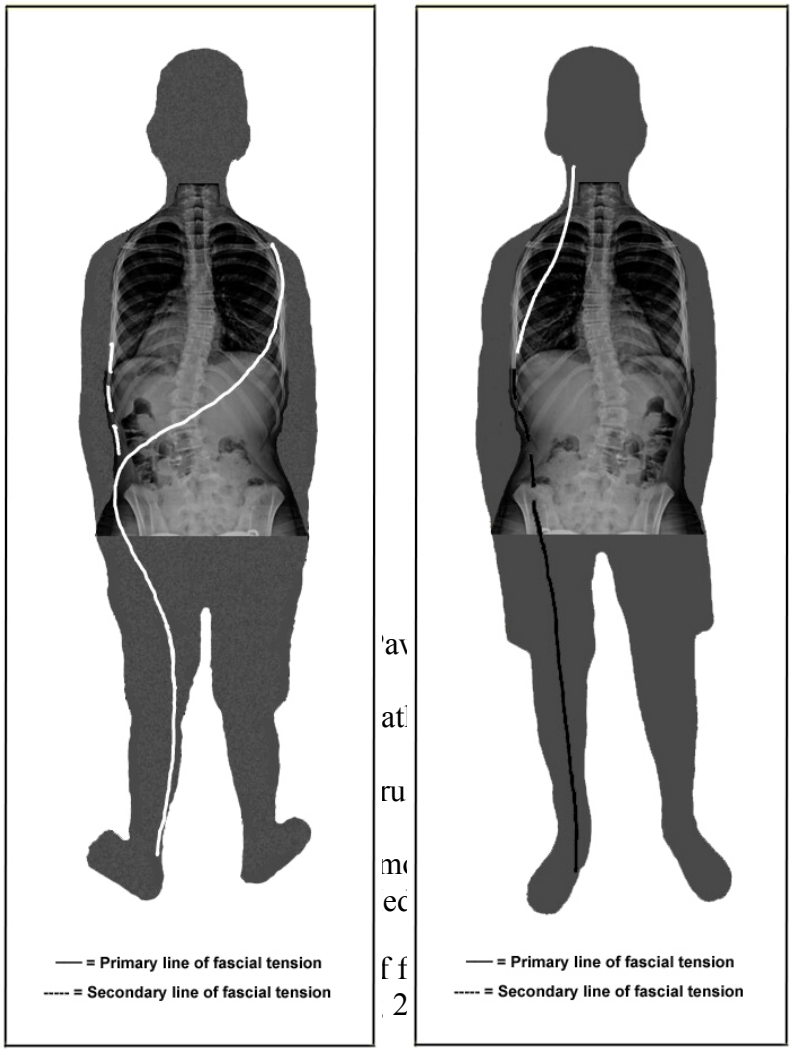
[24] Cho JH, Lee CS, Joo YS, et al. Association between sacral slanting and adjacent structures in patients with adolescent idiopathic scoliosis. Clinics in Orthopedic Surgery 2017;9:57-62.
[25] Zhao Y, Qi L, Yang J, Zhu X, Yang C, Li M. Factors affecting pelvic rotation in idiopathic scoliosis: Analysis of 85 cases in a single center. Medicine (Baltimore). 2016 Nov;95(46):e5458.

Whyte Ferguson's observation about the importance of ligamentous laxity in the development of AIS has been confirmed by other researchers [26] [27] [28] [29]. 22 out of 22 research subjects in the case series referenced above have significant arches in their feet that fully collapse when they are weight bearing. Exercises were not found to be effective to counter the over-pronation, and the degree of over-pronation often differed from one foot to the other so arch supports were prescribed to address the over-pronation.

Imbalances in pronation can be related to pelvic obliquity[30]. Control of over-pronation may be one factor of import in treating AIS. This is one of the factors to be addressed in the proposed research and arch supports will be provided to each of the subjects in the active treatment group.

4. ***Fascial Imbalance***

In a recent literature search, there was no citation to any article that discussed the importance of fascia in treatment of scoliosis with the exception of the case series by Whyte Ferguson cited above. This is not surprising considering that it is only recently that fascia has been identified as a separate organ and viewed as a tissue of import. Treatment strategies to address dysfunction of the fascia are an emerging field. In the normal individual, the spiral fascia are like a double helix that provides balanced support to the spine. It appears that one of these spirals that forms the double helix uncouples and contracts and we hypothesize that this is one of the dynamics that propels



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worsening of the scoliosis. Whyte Ferguson has extensive expertise in fascial release, utilizing a variety of assessment and treatment techniques to address contractions of fascia, most importantly spiral fascia, to successfully treat adolescents with AIS.

Directly addressing the myofascial components of AIS is an entirely new area of focus with regard to treatment of AIS. The DMAMR protocol in the proposed study incorporates fascial release techniques and the subjects will perform exercises that are also designed to release abnormal fascial constriction.

The treatment regimen for AIS that will be employed in the proposed research project is a multifactorial approach based on addressing biomechanical factors 1 through 4 discussed above. These factors may be compensatory to developing spinal curvatures. It is also possible that these factors represent one of the drivers of deformity, propelling worsening of spinal curvatures seen in AIS. The proposed research project is designed to help us learn whether and to what degree countering the influence of these factors can affect the development and progression of AIS. If successful, the rate of bracing and surgery will be significantly reduced, with reduction of pain and improvement of quality of life.

Figure 5. Posterior Spiral; Anterior Spiral. Source: Whyte Ferguson, L.; Adolescent idiopathic scoliosis: The Tethered Spine III: Is fascial spiral the key?. Journal of Bodywork & Movement Therapies. 21 (2017) 948-971.

3. STUDY DESIGN

3.1 Description

A cohort of 28 children and adolescents with scoliosis will receive a treatment protocol including myofascial and articular treatment; home exercises; arch supports, heel lifts and ischial lifts; and bracing as indicated. Treatments will be conducted twice per month for 6 months. A control group of 28 children and adolescents with scoliosis will receive standard care, including standard physical therapy, and bracing as indicated. Outcome measures for the two groups will include data from x-rays taken in the usual course of scoliosis care (every 6 months) at Carrie Tingley Radiology Department at the beginning, and after 6 months of care. The radiologists who will be measuring the spinal curvatures will be blinded. Rib humps will be measured by blinded individuals, at the beginning, and after 6 months of care. The SRS 22 Questionnaire, as a measure of Quality of Life, will be administered by a blinded individual at the beginning, and after 6 months of care. At these same times, subjects will fill out a Pain Scale, also administered by a blinded individual. (X-rays taken every 6 months are part of standard care for children and adolescents with scoliosis. The other measurements are specific to this study.)

4. BLINDING, INCLUSION/EXCLUSION CRITERIA

4.1 – Screening for Eligibility

Potential participants will be drawn from the cohort of current patients at Carrie Tingley Orthopaedic Clinic and will be initially identified and screened by staff at time of new or follow-up visits. Screening criteria for participation includes: (1) age 10-15 years, (2) curvatures ranging from 15 degrees to 30 degrees, and (3) bone growth has not yet completed. Participants may be either female or male. The control and active treatment groups are expected to include participants who are and others who are not wearing spinal braces as a part of their care. English and Spanish speaking subjects will be eligible for participation. Foster children/wards of the state will not be enrolled in the study. Pregnant individuals will not be enrolled in the study.
Principal Investigator, Selina Silva and her medical colleagues will perform the screening for eligibility. They will have access to potential subjects' medical records and will screen for the inclusion and exclusion criteria.

4.2 Inclusion/Exclusion Criteria

Criteria that will define who will be included in the final study sample include age 10-15 years, curvature from 15 to 30 degrees, and the following: (1) Degree of bone growth. Only patients who have not yet completed bone growth as evidenced by the Risser Criteria[31] will be included in the study. (2) Subjects must be willing and available to participate in regular twice-monthly (free) treatments for 6 months. Treatments will take place in Albuquerque or in Taos. Participants' parents or guardians are responsible for providing transportation. (If subjects miss treatments for whatever reason, their data will still be analyzed with the understanding that they did not complete the full treatment protocol.) Preference will be for enrollment of patients exhibiting either double major S-scoliosis or thoraco-lumbar scoliosis. Controls will be matched to the degree possible for age and degree of curvature. Dr. Silva is unblinded and she will assure that the numbers of braced subjects is balanced between the active treatment and control groups by stopping recruitment of subjects to the portions of the groups that are full. Patients enrolled in the study who have a curvature that falls within criteria for bracing at the time of enrollment or during the study will receive bracing plus protocol care. Bracing is a stratification variable for statistical analysis. The proportion of unbraced subjects at the beginning of the study who require bracing at the end of the six month study period will also be used for outcome analysis and comparison between the active treatment and control groups. The criteria for surgery are 40 to 50 degrees of curvature, and no subjects with such severe curvatures will be enrolled. Those who have 20-25 degree curvatures at the beginning of the study will be braced, and there will not be repeat x-rays until the end of the 6 month study. Therefore the study structure and selection process precludes the existence of study subjects who will require surgery during the time of the research. (3) We must have access to data about spinal curvatures from x-rays performed at the beginning of the study and after 6 months (the standard timing for x-rays of children and adults with scoliosis). Pregnant subjects will thus be excluded and this screening will be conducted according to standard procedures at the Radiation Department at Carrie Tingley Children's Hospital. (4) Those subjects in the control group will have access to any treatments that are usual and customary for scoliosis, other than the specific treatment

[31] Hacquebord JH, Leopold SS. The Risser Classification: A Classic Tool for the Clinician Treating Adolescent Idiopathic Scoliosis. Clin Orthop Relat Res (2012) 470:2335-2338.

protocol for this study. They will be prescribed bracing if they meet the criteria for bracing. They may be referred to Carrie Tingley or other physical therapy and will not be excluded from this study if they receive such other treatment. Foster children/wards of the state will be excluded from the study.

4.3 Specific Population

Research will include individuals aged 10 to 15 years, so it will include both children and teenagers.

4.4 Excluded Population

Participants who have spinal curvatures that may involve other disease processes rather than AIS will be excluded. AIS specifically means Adolescent *Idiopathic* Scoliosis. If there is a known disease process that causes the scoliosis, then this person's curvature does not qualify as AIS. Such medical conditions include: Marfan's, Osteogenesis Imperfecta, Congenital scoliosis, Neuromuscular scoliosis, Scheurmanns kyphosis, Spondylolisthesis, and Spondylolysis and possibly other conditions that may contribute to scoliosis such as Cerebral Palsy, and Juvenile Rheumatoid Arthritis.

Measures will be taken to translate for any children or teenagers who are Spanish speakers. Spanish versions of consent forms, for example, can be provided, and Dr. Whyte Ferguson is fluent in Spanish. (Once the English versions of Recruitment brochures, Consent, and Assent Forms are approved, we will proceed to complete Spanish versions of these documents.)

We will also be excluding children that fall outside of the age range 10-15 years of age and those adolescents that are skeletally mature will also be excluded. Families that are unable to get treatment twice per month in Albuquerque or Taos will also be excluded. Potential participants that speak a language other than Spanish or English will be excluded.

5. NUMBER OF SUBJECTS

5.1 Multi-center Study

This is not a multi-center study. The proposed study will have patients treated at various locations, but all with the same team of investigators associated with the University of New Mexico Hospital. This study does NOT involve multiple coordinating institutions. All recruitment and pre and post assessments will take place at Carrie Tingley Orthopaedic Center. We will also use the x-ray data from x-rays taken at Carrie Tingley which will be part of screening for criteria of inclusion/exclusion. But the intervention will take place in separate buildings for the following reasons: We will treat children and adolescents at the CTSC clinical rooms between 9 and 5 on weekdays in Albuquerque Also, since Dr. Whyte Ferguson is providing the intervention treatment and since her home and office are in Taos/El Prado, her private office is also available for scheduling those subjects who would find it more convenient to travel to Taos including those who would like to be scheduled for

treatment on Saturdays. There will be minimal contact of subjects with Colonias Chiropractic Center (Taos/El Prado) staff, except for scheduling and use of hydrocollators So the centers per se do not have a role in the research. Dr. Whyte Ferguson will provide the evaluations, care, exercise instruction, etc., in both locations.

5.2 Number of Subjects

Fifty-six subjects will be recruited for this study. Twenty-eight will be randomly assigned to the treatment group and twenty-eight will be assigned to the control group.

5.3 Sample Size Justification

Comparable scoliosis studies have achieved statistically significant outcome measurements with comparable numbers of subjects. Schrieber et al. (2016) planned their 6-month study of change in Cobb angles assuming an effect size of 0.50 with 0.6 correlation between repeated measures. The difference they observed as >1.0. Our pilot study will employ 28 participants in each study arm, and with this sample size an effect size of 0.72 will have 80% power (two-sided $\alpha = 0.05$). Therefore, even though the proposed work is a pilot study it has sufficient power for the primary outcome variable.

6. STUDY TIMELINES

6.1 Description

Individual subjects participation will be for 6 months.
*It is unlikely to take more than 2 months to recruit the 56 required subjects.
*Orrin Myers expects that statistical analysis following the end of treatment and the completion of the final measurements and questionnaires, will require 20 hours of his time and he has requested that we allow 2 months for this analysis.

7. STUDY ENDPOINTS

7.1 Primary and Secondary Endpoints

The primary study endpoints are changes in Cobb angle and rib hump angle at 6 months. The secondary endpoint is improved quality of life at 6 months measured by pain score and the SRS22 instrument. With 2 months for recruitment and 6 months for the treatment intervention, and the collection and analysis of data, the study should be completed within the 1 year grant period.

7.2 Safety monitoring will be described in section 14. If there are treatment reactions that are significantly worse than muscle soreness for 24 to 48 hours, monitored every 2 months during the active treatment regimen, the research team will consult and consider early termination of the study. As mentioned earlier, research over the last 40 years has concluded that more severe treatment reactions are very rare and are almost always associated with failure to

diagnose or cervical manipulation and, as described earlier, neither of these factors would apply to this study design and treatment regimen.

7.3 Exploratory Endpoints

Decrease in incidence of patients who are initially unbraced but then require corrective bracing and decrease in incidence number of patients who require corrective spinal surgery are exploratory end points.

8. RESEARCH SETTING

8.1 Research Sites

Research team will conduct research at Carrie Tingley Hospital, Outpatient Center, Department of Pediatric Orthopaedics. All assessments including, measurements, and questionnaires will be conducted at this site. Data from x-rays taken every 6 months, the beginning and ending of the treatment period, will be accessed at Carrie Tingley and entered as data in this study

8.2 Recruitment Site

Recruitment of potential subjects will take place at Carrie Tingley Hospital, Outpatient Center, Department of Pediatric Orthopaedics.

8.3 Procedures Site

Active treatment for this study will be conducted at the CTSC clinical rooms and at the co-investigator's private practice location, Colonias Chiropractic Center, 98 State Hwy 150, Suite 9, Taos/El Prado, NM. Those in the active treatment group will be able to choose the location that is most convenient for them. **8.4 Community Advisory Board**

N/A

8.5 Research Outside of UNM

N/A

9. RESOURCES AVAILABLE

9.1 PI /Study Staff Qualifications

Principal Investigator: Selina Silva, MD.
Associate Professor**.** Specialty: Pediatric Spine**.** Medical School: University of Colorado**.** Residency: University of New Mexico (UNM)**.** Fellowship:Pediatric Orthopaedic; University of Michigan

Dr. Selina Silva joined the Carrie Tingley Hospital (CTH) division of pediatric orthopaedics in September 2011. She is currently the Medical Director at CTH and is an Associate Professor in UNM's Department of Orthopaedics & Rehabilitation. She received her medical degree from the University of Colorado, in her hometown of Denver in May 2005 and completed her residency training in Orthopaedic Surgery at UNM in June 2010. Following her residency training, Dr. Silva temporarily left New Mexico to complete a yearlong fellowship in pediatric orthopaedic surgery at the University of Michigan in Ann Arbor. She is interested in the sub-specialties of Early Onset Scoliosis, Hip Dysplasia, Cerebral Palsy and Bone Health. Dr. Silva plans to continue her research endeavors in the areas of Fracture Management, Scoliosis, and Hip joint disorders.

Professional Memberships and Certifications
Dr. Silva is board certified by the National Board of Medical Examiners and the American Board of Orthopaedic Surgery. She is a member of the Pediatric Orthopaedic Society of North America, American Academy of Orthopaedic Surgeons, American Medical Association, Ruth Jackson Orthopaedic Society, Western Orthopaedic Association, Association of Women Surgeons, Alpha Omega Alpha Honor Medical Society and Phi Beta Kappa Honor Society.

Co-Investigator: Lucy Whyte Ferguson, D.C.
Cornell University, Ithaca, New York; BA 1969. Dean's List, Seal and Serpent Scholastic Honorary Society. Los Angeles College of Chiropractic, Whittier, California. DC 1981. Summa Cum Laude.
Private practice, Silver Spring, Maryland 1982 to 1994. Private practice, Taos, New Mexico 1992 to Present. Taos Pueblo 1992-2014. UNM Medical School Pain Center 2013 to Present.

Faculty member, UNM Department of Neurosurgery. Myofascial expert, UNM Project Echo: Chronic Pain and Opioid Management Clinic. Licensed to practice in New Mexico.

Professional Awards
1996 Janet Travell, M.D. Soft Tissue Pain Management Award, American Academy of Pain Management

Publications - Articles
Treating Shoulder Dysfunction and "Frozen Shoulders" Chiropractic Technique, Vol 7, No.3, pp. 75-81, August 1995.
Knee pain: Addressing the interrelationships between muscle and joint dysfunction in the Hip and pelvis and lower extremity. Journal of Bodywork and Movement Therapies, Volume 10, Issue 4, October 2006, pp. 287-296
Myofascial Pain: A Manual Medicine Approach to Diagnosis and Treatment, by Lucy Whyte Ferguson, D.C. and Ben Daitz,M.D., The Pain Practitioner (published by the American Academy of Pain Management) Volume 22, Number 2, Summer 2012.
Adult Idiopathic Scoliosis: the Tethered Spine; Journal of Bodywork and Movement Therapies, Volume 18, No. 1, pp. 99-111, January 2014.
Idiopathic Scoliosis: the Tethered Spine II, post-surgical pain; Journal of Bodywork and Movement Therapies, Volume 18, No. 4, pp. 501-513, October 2014.
The Importance of Interdisciplinary Care in My Professional Life. The Pain Practitioner

(published by the American Academy of Pain Management) Volume 26, Number 3, June/July 2016, p.13.
Adolescent Idiopathic Scoliosis: the Tethered Spine III: Is Fascial Spiral the Key? Journal of Bodywork and Movement Therapies, Volume 21, No. 4, pp. 948-971, October, 2017.

Publications - Books
Lippincott,Williams and Wilkins Publishing Company published interdisciplinary text: **Clinical Mastery in the Treatment of Myofascial Pain** edited by Lucy Whyte Ferguson and Robert Gerwin, M.D. Whyte Ferguson wrote chapters on Frozen Shoulders and Shoulder Dysfunction, and Hip and Groin Pain and co-authored the chapters on Whiplash Injuries and on Lower Back Pain, and Heel Pain for this text. Book was published in 2005. Released in Portuguese in 2007. Released in Russian in 2008.

Publications – Chapter Contributions:
Myofascial Pain Syndrome: The Team Approach; chapter published in Integrative Pain Management edited by Robert A. Bonakdar and Andrew W. Sukiennik, Weil Integrative Medicine Library, published by Oxford University Press, 2016.
(Credentialed through University of New Mexico Department of Neurosurgery to treat adults and children from age eight on up.)

Additional Staff Resources
Dr. Silva will use a medical colleague to assist in recruitment of subjects, and blinded nurse practitioners to measure rib humps and administer Pain and Quality of Life Questionnaires. Data regarding degree of curvature for this study will be drawn from the x-rays that are normally taken every 6 months as standard care for monitoring children and adolescents who have scoliosis. These x-rays are taken in the Radiology Department at Carrie Tingley Hospital. The radiologists who read these x-rays will be blinded as to which subjects are in the control group and which subjects are in the active treatment group.

9.2 Medical Decision-Making

Principal Investigator, Dr. Silva will be responsible for medical decision-making and ordering and evaluating diagnostics and therapeutics. Co-Investigator, Dr. Whyte Ferguson will make decisions within the protocol of treatment that is being studied and applied to the active treatment group.

9.3 Other Resources

Dr. Selina Silva and colleagues see 15 to 20 children and adolescents with scoliosis per week. Considering the inclusion and exclusion criteria, it is likely that they will be able to recruit the 56 required subjects within 2 months. From 127 to 170 children and adolescents with scoliosis, it is likely that 56 suitable subjects can be recruited.
With 2 months for recruitment, 6 months for active treatment, 1 month devoted to measurements and questionnaires, and 2 months for statistical analysis, we should be able to complete the research within 1 year.

Written instruction and in person meetings with the nurse practitioners will be conducted so that the rib hump measurements will be made in a consistent fashion. Administering Pain questionnaires and Quality of Life questionnaires will be reviewed with the nurse practitioners as well. They or a recruited resident will input this data into the RedCap system.

10. PRIOR APPROVALS

10.1 No approvals will be required prior to commencing the research.

10.2 Departmental Review Form

Dr. Silva's form has been submitted as a separate supporting document.

10.3 X-rays

The study will not be performing x-rays of subjects but will pull data from the x-rays that are taken every 6 months, which are the standard of care for monitoring children and adolescents with scoliosis. No other ionizing radiation will be administered in the course of this study. (The radiation unit at Carrie Tingley that will have taken the standard x-rays on these subjects has Radiation Safety Certification.)

10.4 Biological Specimens / Drug Attachments

N/A

11. MULTI-SITE RESEARCH

N/A: All research measurements and evaluations will be conducted through Carrie Tingley. The protocol intervention will be conducted by the Co-Investigator, Whyte Ferguson at a standard chiropractic office in El Prado/Taos and at the CTSC clinical rooms in Albuquerque.

12. STUDY PROCEDURES

12.1 Collaborating Sites

All research measurements and evaluations will be conducted through Carrie Tingley. Co-Investigator will perform the protocol intervention at CTSC clinical rooms at University of New Mexico in Albuquerque and in her private office in Taos/El Prado, NM.

12.2 Study Procedures, Assessments, Activities

Screening: Potential subjects will be screened to make sure they meet the study's inclusion criteria: age 10 to 15, curvature from 15 to 30 degrees, and not having completed bone growth. Pregnancy will preclude participation, because we will not have access to the x-ray data necessary for this study if the potential subjects are pregnant. Pregnancy screening and any necessary testing for pregnancy will be performed by the Radiation Department according to their standard procedures. Subjects will also be screened to exclude individuals who have

other significant medical conditions (described above) contributing to spinal curvature because the appropriate subjects are those with curvatures categorized as AIS alone. Subjects must speak either English or Spanish.

Consent:
The consent process will be conducted by Dr. Silva and colleagues in a private clinic room. It will be made clear that potential subjects will not lose any of their existing care if they decide not to participate.

Randomization:

Dr. Silva and her medical colleagues will conduct the random assignment of subjects to the active treatment and the control group. These colleagues are listed as study members. The actual randomization will be performed by the computer. Dr. Silva will close recruitment to the treatment or control group, as necessary, to assure a balance of braced and unbraced subjects in each group. Dr. Silva and her colleagues have no stake in the success or failure of the active treatment intervention, and Dr. Whyte Ferguson, who does have a stake in proving out the usefulness of the active treatment intervention, will have no role in the randomization process (nor in selection, consent, measurements at the beginning of the research, measurements at the end of the 6 month treatment/control period, storage of data from these measurements, and statistical analysis of the data that has been stored in REDCap).

Added Cross-Over:
The COVID epidemic has had a negative effect on recruitment. In the last 2 months of recruitment, Dr. Silva will be offering participation in the active treatment group to subjects who have completed their participation in the control group, as long as they continue to meet the Screening Criteria described above. The x-ray measurements made at the end of their control group participation will be used as the x-ray measurements for the beginning of the active group participation. The data from rib prominence measurements and questionnaire responses collected at the end of the control group participation will also be used as the beginning data for the active treatment group participation. In other respects, the study procedures will be the same for the cross-over subjects as for those originally recruited to the active treatment group. In analyzing data at the end of the study, comparisons may be made between each cross-over subject's data at the end of their control group participation and the data collected at the end of their active treatment group participation.

After selection of potential participants, consent procedures and randomization of treatment and control group, the following procedures will be conducted:

1) X-ray evaluation will be conducted on the participants' usual 6 month schedule as part of their standard care. Note that the X-rays are not provided under this study but are part of standard medical care of these children and adolescents with scoliosis at Carrie Tingley. The x-ray curve measurements form the baseline measurements for the study.

2) Midlevel Provider will measure rib humps and will administer SRS22 Quality of Life Questionnaire and Pain Scale to control group and active treatment group at beginning of study. The rib hump measurements will assess one aspect of the deformity that results from scoliosis. The questionnaires have been applied in other research on scoliosis and are recommended as components of high quality research by the SRS-SOSORT research recommendations.
3) Active treatment group will be examined with regard to joint and myofascial dysfunctions, muscle strength and weakness, and joint dysfunction and ligamentous laxity will be assessed with Beighton scale. Participants will also be assessed with regard to over-pronation, and whether the pelvis is balanced while seated and standing. These (free) assessments will determine the design of treatment interventions.
4) Active treatment subjects will then receive (free) treatment twice per week for 6 months, including joint manipulation to thoracic and lumbar spine and pelvis, and mobilization of the cervical spine as indicated as well as muscle trigger point and myofascial and fascial release. Heel or ischial lifts and/or arch supports will be provided as indicated. Home exercises will be prescribed with exercise equipment provided for free. A small ball for rib mobilization will be provided to each participant. A doorway stretching (or chin-up) bar will be provided that fits securely over the door frame and requires no installation. Some homes, particularly adobe homes, do not have door frames, so stretching or chin-up bars will be provided that can be installed. Subjects will keep a log of compliance with exercises and use of heel and/or ischial lifts. The logs of compliance will be used to help interpret research results.
5) 6 months after the initial assessments, both the active treatment group and the control group will be re-evaluated with x-rays (again provided as part of standard care at Carrie Tingley Radiology), rib hump measurement, and SRS22 and Pain Scale and this completes collection of data for assessment of the results of the intervention.
6) Control group participants will be free to pursue standard physical therapy if they so desire.
7) Research results will be analyzed and written up and information will be shared with participants. Analysis will be completed with the goal of writing an article for publication.
8) SRS22 (Quality of Life) and Pain Scale documents and logs of exercise compliance will be submitted as separate attachments.
9) The exercise equipment includes: over the door hanging bar and ball. Heel lifts and ischial lifts, arch supports are also provided as part of treatment protocol.
   Treatment tools used by the treating doctor include: the activator adjusting instrument and a standard triangular reflex hammer, as well as hydrocollator packs.
   All of this equipment and these devices are being used in this research project but are not being studied for safety and effectiveness. This equipment and these devices are already used in standard chiropractic care and physical therapy.

12.3 Prospective Data Sources

N/A

12.4 Study Activities Location and Timing

Already described in section 11 and 12.2

12.5 Chronological Order of Procedures and Interventions

Already described in section 12.2.

13. DATA ANALYSIS

13.1 Data Analysis Plan, Statistical Procedures

Our primary study outcomes are change in Cobb angles and rib hump angles. Schrieber et al. (2016) found that changes in Cobb angles were associated with patient height and weight in addition to treatment. Therefore, we will use a linear mixed model approach to account for repeated measures and adjust for height and weight. In these analyses the time x treatment interaction tests whether pre/post change is different for the two study arms. Pain and quality of life measures will be analyzed using a similar approach. We will examine distributions of outcome variables to determine if transformations are needed to improve adherence to analysis assumptions. Fisher exact tests will be used to assess whether frequency of corrective bracing or spinal surgery is different for the two study arms. As this is a pilot study we will not adjust alpha (0.05) for multiple comparisons. Summary means, standard deviations, frequencies and percentages will be computed.

13.2 Power Analysis

Schrieber et al. (2016) planned their 6-month study of change in Cobb angles assuming an effect size of 0.50 with 0.6 correlation between repeated measures. The difference they observed as >1.0. Our pilot study will employ 25 participants in each study arm, and with this sample size an effect size of 0.72 will have 80% power (two-sided $\alpha = 0.05$). Therefore, even though the proposed work is a pilot study it has sufficient power for the primary outcome variable.

14. SUBJECT SAFETY MONITORING

14.1 Who will be monitoring safety of subjects in the treatment group

The individuals who will receive reports of complaints from the subjects in the treatment group include Dr. Whyte Ferguson, the individual interacting with the subjects approximately every 2 weeks and performing the treatment intervention during the active treatment period. Dr. Whyte Ferguson will perform pain scale reporting by subjects on every visit. The results

of this reporting will be transferred (in coded form) to the Principal Investigator, Dr. Silva and any increase in the pain scale will be highlighted for Dr. Silva's attention. Anything beyond increased muscle soreness for 24 to 48 hours (the maximum expected treatment reaction) will be highlighted also, whether the increased pain is reported as related to the intervention or not, so that Dr. Silva can make her own assessment. Dr. Silva's office is also listed as the contact for any concerns raised by parents or subjects, so Dr. Silva will be in charge of assessing the nature of any of these concerns and prescribing appropriate medical care. Dr. Silva has no stake in the success or failure of the treatment intervention and she will be providing medical oversight.

14.2 **Safety information that will be collected and monitored**

Pain scale responses from each visit will be collected by Dr. Whyte Ferguson and transferred to Dr. Silva, and the pain scale responses will be tracked and summarized for each participant every 2 months during the 6 month treatment intervention. These summaries will also be reviewed by Dr. Silva, who will be providing medical oversight.

14.3 **Frequency or periodicity of review of data**

The summaries of pain scale responses will be provided every 2 months of the 6 month intervention period, for the review of Dr. Silva. Every two weeks, the base data of the pain scale responses of subjects on each visit will be supplied to Dr. Silva with an alert regarding any increase in pain level, and any response indicating a negative reaction that involves more than the expected increased muscle soreness for 24 to 48 hours.

14.4 **Plans for review of scientific literature and data from outside sources that may inform the safety or conduct of the study**

The relevant scientific literature has already been consulted regarding the expected safety of the study procedures and this review has informed the planned procedures incorporated in the treatment protocol.

14.5 **The procedures for analysis and interpretation of the safety data**

Dr. Silva is very experienced in reviewing pain data reported by the subjects of this study, just as she reviews pain scale data in her routine care of children and adolescents in her regular clinical practice at Carrie Tingley Childrens' Hospital.

14.6 **The conditions that would trigger the suspension or termination of the research**

If any child suffers a rib fracture or herniated disc as a result of study procedures, the research should be suspended or terminated. Such complications are very rare even in adults and are almost never reported in the care of children or adolescents. The procedures used in this study are performed gently, well within the subjects' pain tolerance.

14.7 **The plan for reporting findings to sponsor, investigators, and HRRC**

Dr. Silva will refer any significant pain increase potentially related to the treatment intervention, as reflected in the data summaries for each subject in the active treatment group provided every 2 months during the 6 month intervention period, to both the sponsor(s) and HRRC.

It should be noted that the maximum expected reaction to the treatment regimen is self limited muscle soreness for 24 to 48 hours. Because this reaction is different from the subjects daily life experience, the intervention is considered minor risk rather than minimal risk. But muscle soreness for 24 to 48 hours is well within the subjects frequent experience, when they start a new exercise or sport. For this reason, the expected worst case scenario is not generally of concern to the subjects or their parents.

15. WITHDRAWAL OF SUBJECTS

15.1 Non-Consensual Subject Withdrawal

There are no expected circumstances under which subjects may be withdrawn from research without their consent. If participants receiving the active intervention do not perform their exercises or do not use heel lifts and arch supports, records of compliance will be kept and used in the interpretation and assessment of feasibility. (It is Dr. Whyte Ferguson's experience that she can often tell if subjects have slacked off on their performance of exercises, and identifying this and providing encouragement are part of the active intervention.) Subjects will not be dropped from the study for failure to perform exercises. If subjects selected for the active intervention do not come to treatment visits, attempts will be made to make up the missed sessions. If subjects drop out early in the process, their consent is implied by dropping out, and it may be feasible to continue the enrollment process and fill out the active treatment group. Participants may withdraw from the study at any time, and may notify either Dr. Silva or Dr. Whyte Ferguson of their desire to do so, or their withdrawal may be inferred from their lack of attendance. Participants who drop out early may be replaced if it is feasible to do so. Data on those participants who are not replaced will be retained and analyzed with the decreased treatment considered in the analysis (unless the subject directs that their data be removed from the study) and this is part of the assessment of feasibility. It will be made clear to participants that they will lose none of their eligibility for standard care through Carrie Tingley Orthopedic Clinic as a result of their withdrawal. The number of subjects enrolled in the study has included the expectation of some attrition, with the likelihood that it will still be possible to analyze the statistical significance of the results. Again, this is part of the assessment of feasibility.

15.2 Orderly termination / Safe withdrawal

N/A. Not required; subjects can terminate chiropractic care with no safety repercussions.

15.3 Partial Withdrawal

If subjects in the active treatment group fail to come for treatment of fail to perform exercises, their data will be interpreted with this taken into consideration. If they choose to drop out of the study, this is allowed, and the data already collected will be used.

15.4 Withdrawn Subjects Disposition of Data

If a subject withdraws, the data already collected will be used in the analysis unless the subject specifically directs the removal of this data from the study record.

15.5 Withdrawal Procedures and Limitations

Subjects are requested to notify investigator or coordinator if they wish to withdraw from the study. All subjects are free to withdraw at any time, without limitations.

16. DATA MANAGEMENT/CONFIDENTIALITY

Data forms will be kept in a locked file cabinet in a locked office.
Project data will be coded into the HIPPA-compliant installation of REDCap maintained by the UNMHSC. A limited analytic file will be used for data analyses conducted on UNM computers. Research records and data collected will be retained until research subjects reach 22 years of age.

16.1-16.4 Data Sharing

N/A No data sharing

16.5 Research team access

Dr. Silva will place a note in each subject's chart indicating that they are subjects in this research study. Any individual rendering medical or other care to these research subjects will thus have access to this information simply by consulting their medical record.
The blinded nurse practitioners will access the data on the patients x-rays and will have the information about rib hump measurements and the results of both questionnaires and they or a Resident will input this data into the REDCap system. After this, the raw data and any records of medical visits of treatment of active treatment subjects during the treatment period will be kept in a locked file in Dr. Silva's office and only the unblinded medical practioners will have access to this part of the medical record. Dr. Whyte Ferguson will not have access to these data but will have access to beginning x-ray images of study subjects in order to plan interventions.

Records of Off-Site Treatment

What will take place at the UNM CTSC clinical rooms in Albuquerque and Dr. Whyte Ferguson's Taos/El Prado office is the examination and treatment of the active treatment subjects. Records of the examination and treatment sessions will be maintained but coded and kept in the secure electronic record that Dr. Whyte Ferguson uses to keep records of all of her

patients. She will need to have continuing access to this information so that she can refer back to prior visits when making clinical decisions about current and ongoing treatment. Treatment records would ordinarily be entered into the patient's regular UNM record, but this obviously cannot be done during the study because it would reveal who is and who is not in the active treatment group versus the control group, and would thus potentially destroy the blinding. These records are not the measures that will be used in the monitoring and statistical analysis of treatment results between active and control groups. They are not the Data for this study, so they will not be deposited in the REDCap system. As soon as the study is complete, Dr. Whyte Ferguson will electronically enter the treatment notes into the Clinical Notes section of each active subject's UNM medical record. Dr. Whyte Ferguson uses this same procedure to complete her UNM Pain Center treatment notes remotely on her computer and transfer these notes to the patient's UNM electronic patient record.

16.6 Access, use, or disclosure of direct identifiers

This research project does not require access, use, or disclosure of direct identifiers except during initial screening and access required for providing medical care to study participants by unblinded medical personnel. After initial screening and consent procedures, each participant will be identified by a numerical code. Dr. Silva will have the key that connects direct identifiers with that code and this will be stored in a locked file in her office. All of the data as it is deposited in REDCap will be identified using the code, rather than direct identifiers.

16.7 Access, use, or disclosure of PHI

PHI will only be used during the screening process. Therefore, we are requesting a waiver of HIPAA authorization: Adequate written assurances that the protected health information will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research study, or for other research for which the use or disclosure of protected health information for which an authorization or opportunity to agree or object is not required by 45 CFR 164.512.

16.8 Note whether data is publically available

Data will not be publically available.

16.9 Data does not include sensitive information or information requiring additional protections.

16.10 Certificate of Confidentiality

Once the Certificate of Confidentiality is obtained after IRB approval, the PI will submit a Modification to revise consent to reflect Certificate of Confidentiality.

16.11 Steps taken to secure data

After data is initially collected (measurements, questionnaires) it will be kept in a locked file in a locked office. The Nurse practitioners or a resident will be trained to input the data to the REDCap system. A password protected computer will be used for this process and data will

be encoded and the participants will be assigned numbers. Other than the secure REDCap system, there will be no transmission and there will be no transport of data.

16.12 Coding of Data
The participants will be assigned numbers, and the code will be kept in a secure locked file in the Principal Investigator's office, a locked office.

16.13 Quality Control
X-ray measurements will be performed by blinded radiologists, in the normal course of their work. The quality of the rib hump measurements will be maximized by the training process with the nurse practitioners. The review of procedures for the questionnaires prior to their administration, and the review of the questionnaires by the nurse practitioners prior to the input of the data to the REDCap system will assure that the participants have completed the questionnaires properly.

Dr. Silva, a trained researcher, will set up the REDCap file and will train the nurse practitioners in data collection and data input into REDCap. The Biostatistician will be asked to evaluate the quality of the data early on and advise Dr. Silva about any needed changes to improve data quality.

16.14-16.15 Data and specimens will not be transported to outside entities. Data will only be transferred within the UNM system via the REDCap system.

16.16 Audio and Video Recording
Two or three subjects in the active treatment group will be asked to allow video of 4 treatment sessions, 2 at the beginning of treatment and early in treatment, 1 halfway through the study, and 1 at or near the last treatment session. The images will be altered so that faces are obscured and unidentifiable. The purpose of the videos will be to provide instruction on the modes of treatment involved. These subjects will be asked to give permission for the videos and no subject will be subjected to video without consent. The subjects will be offered the opportunity to review the videos, and if they have any objections, videos will be altered to address their concerns. It is not expected that subjects will request that videos be deleted because they will not be identifiable. The only other person who will be identifiable in the videos is the co-investigator, Dr. Whyte Ferguson, who will be providing the active treatment. Subjects will be offered the option in the consent/assent process to allow or disallow being requested to have video taken.

16.17 Photographs
The only images that will be in use during the research are printouts of the most recent scoliosis x-rays for each participant in the active treatment group. The co-investigator, Dr. Whyte Ferguson, will be using the images in planning and conducting the active treatment of the subjects. The notebook with these images will be kept secure, and locked whenever not actually in use during treatment sessions.

16.18, 16.19 How Long Research Record Will be Maintained

Research record will be maintained until the subjects are 22 years of age per the following policy: HSC-R-801 PR.1 "Research Data and Materials Retention Policy".

16.20 Even though HIPAA protected information will only be used for screening purposes, the data from this research will be retained for a minimum of 6 years after each subject signed an authorization and until subjects reach 22 years of age.

17. DATA AND SPECIMEN BANKING

17.1 Repository for Data, Specimens

The data regarding x-rays of the subjects in both the active treatment group and the control group will be stored in the regular secured patient files at Carrie Tingley Children's Hospital, as part of their files in the University of New Mexico medical system. The data regarding rib humps, and responses to Pain and Quality of Life Questionnaires will be entered into the REDCap repository system. The data will be encoded and will be aggregated for statistical analysis. The data uploaded into REDCap will be de-identified. The data will not be stored for any future unspecified research.

17.2 Banking of data in multi-center study

N/A because this is not a multi-center study. All of the data for monitoring the status of each subject in the active treatment and control group will be collected at Carrie Tingley Children's Hospital. This data will be retained and analyzed using the REDCap system. The data will be retained in the REDCap system for time sufficient to respond to any queries around securing publication of article or articles in journals. The data will not be retained or banked for unspecified further research. The data will be retained until the subjects reach age 22. Then the data will be transferred to the patient's secure UNM medical record or destroyed. The examination and treatment notes of the active treatment subjects who are treated in Taos/El Prado, New Mexico, at Dr. Whyte Ferguson's private office, or at CTSC clinical rooms in Albuquerque will be coded and stored securely in Dr. Whyte Ferguson's computer and electronic health records and these records will be transferred back to the subjects' secure UNM medical files.

18. RISKS TO SUBJECTS

18.1 Reasonably foreseeable risks

Safety of Chiropractic Care

Safety data on risks of pediatric chiropractic care relate principally to missed diagnoses. Because these subjects will be co-managed with medical staff at Carrie Tingley throughout, the risk of a missed diagnosis is minimal. Other risks from pediatric chiropractic care are generally minimal and generally include a low level of soreness that persists for only 24 to 48

hours[32] [33] [34] [35] [36] [37] [38]. The chiropractor will refer subjects in the active treatment group for medical care if any untoward symptoms arise, either as a result of procedures performed, or simply because symptoms are reported during the active treatment sessions. Dr. Whyte Ferguson will fully communicate with them about her concerns. They will take care to keep the records of these visits separate from the medical record that the blinded nurse practitioners could access during the research period. All of the care that these subjects require will take place without the participation or knowledge of the blinded nurse practitioners. The measurements and questionnaires (after the data is entered in REDCap) and any data about medical care required during the active treatment of study subjects will be stored in a locked file in Dr. Silva's office, so these records will not be accessible to the blinded nurse practitioners. The data uploaded into REDCap will be de-identified. The Co-Investigator who will be performing the treatment of the active treatment subjects, has treated children and adolescents throughout her 37-year chiropractic career without any significant complications other than muscle soreness that may last from 24 to 48 hours. She was even able to help treat the pain of a child with scoliosis due to osteogenesis imperfecta without any complications, and she significantly helped this child with pain reduction. Note that the Co- Investigator's credentialing through the UNM Department of Neurosurgery does not allow her to perform cervical manipulation (as opposed to mobilization) so any risks that might be attendant to such procedures will not be applicable to the treatment of subjects in this research study. Hydrocollator therapy will be applied to warm the muscles and make it easier to perform soft tissue release procedures. Plenty of towels will be placed between subjects and the hydrocollator packs, and a call bell will be provided to subjects during hydrocollator application. The Co-Investigator or another staff member will be within earshot of any subject who is receiving hydrocollator therapy. Hydrocollator therapy has been used as a regular part of Dr. Whyte Ferguson's care of patients for the past 37 years and she is not aware of any injuries that have occurred from hydrocollator therapy.

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[32] Alcantara J, Ohm J, Kunz D. The safety and effectiveness of pediatric chiropractic: a survey of chiropractors and parents in a practice based research network. Explore (NY). 2009 Sep-Oct;5(5):280-5.

[33] Carnes D, Plunkett A, Ellwood J, et. al. Manual Therapy for unsettled, distressed and excessively crying infants: a systematic review and meta-analyses. BMJ Open. 2018 Jan 24;8(1).

[34] Dissing KB, Hartvigsen J, Wedderkopp N et. al. 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.

[35] Hawk C, Schneider MJ, Vallone S et. al. Best practices for chiropractic care of children: a consensus Update. J Manipulative Physiol Ther. 2016 Mar-Apr:39(3):158-68.

[36] Humphreys BK. Possible adverse events in children treated by manual therapy: a review. Chiropr Osteopat. 2010 Jun 2;18:12.

[37] Todd AJ, Carroll MT, Robinson A, et. al. Adverse events due to chiropractic and other manual therapies for infants and children: a review of the literature. J Manipulative Physiol Ther. 2015 Nov-Dec;38(9):699-712.

[38] Vohra S, Johnston BC, Cramer K, et. al. Adverse events associated with pediatric spinal manipulation: a systematic review. Pediatrics. 2007 Jan;119(1):e275-83.

The extremely unlikely events of a child suffering a rib fracture or a herniated disc are listed as reasons for terminating the research study. These events have rarely if ever been reported in children (although they have been reported in adults) and would generally indicate a pre-existing condition such as low bone density. If either of these events were to occur, this would indicate faulty screening or inappropriate forcefulness of treatment procedures.

Risk of Loss of Privacy
Note that almost all research includes confidentiality risks. Since the data will be stored in the patients' UNM files and will be coded and stored in the REDCap system, confidentiality risks are no more than any patient with a UNM file faces. The treatment records of the intervention sessions will be stored in a similarly secure site until the completion of the study when they also will be transferred and stored in the patients' UNM files. These are the measures which will be taken to minimize the risk of breach of confidentiality. It will help to have the data uploaded into REDCap to be de-identified.

Risks Related to Use of Heel Lifts, Arch Supports, Ischial Lifts, Small Balls, Stretching (chin-up) Bar
Dr. Whyte Ferguson is not aware of any injury suffered from the use of heel lifts, arch supports, ischial lifts, or small balls or stretching bars and these measures have been a standard part of her care of patients for at least 18 years. Subjects are instructed not to perform exercises if they are painful in any way. The stretching or chin-up bars are not being used for chin-ups. Subjects are instructed to keep their feet on the floor and to let the knees bend and to bow the torso anterior and posterior on either side to gently stretch the fascial tension that spirals around the torso in AIS. They are instructed that fascia stretches better when stretching is performed slowly and gently. It is possible to have some muscle soreness after stretching but any soreness would be expected to subside within 24 to 48 hours.

Procedures that may have unforeseeable risks
While the combination of treatment procedures in the treatment protocol form a novel approach to the treatment of AIS, each of the procedures have been part of the usual and customary treatment procedures in chiropractic (and physical therapy) practices for many decades. The only exception is the fascial release procedures, and these are soft tissue release procedures that have been developed over the last 20 to 30 years, and some of these techniques have been developed more recently, as the field of fascial treatment has developed. Because fascia releases best when release procedures are performed slowly and gently, it is not likely that these newer procedures will cause pain or injury. It is unlikely that there are significant unforeseeable risks for these procedures, because soft tissue release procedures are not generally considered to be risky under most circumstances, except for possible muscle soreness for 24 to 48 hours.

18.3 Risk to embryo or fetus
The only procedure linked to this study (but not performed under the study) that would place a fetus at risk would be an x-ray. According to Carrie Tingley Hospital Radiology Department regular screening procedures, X-rays will not be performed on any adolescent who has become pregnant. This study is not performing the x-rays but is simply drawing the data from

the X-rays that are part of the usual care of scoliosis patients, every 6 months, and the medical necessity has been considered to outweigh the risks of that exposure to ionizing radiation.

18.4 Risks to others who are not subjects
N/A There are no risks expected for anyone who is not a subject.

18.5 Describe steps to minimize the probability or magnitude of risks
The procedures employed in the active treatment protocol are performed very gently and are always conducted within the tolerance of the subject. These are the steps that minimize the probability and magnitude of risks.

19. POTENTIAL BENEFITS TO SUBJECTS

19.1 Potential Benefits
If the research results in slowing progression of curvature, or if the intervention results in decreasing the curvature, these results may persist after the completion of the study. Even if no further treatment is accessed by the subjects, and if worsening of the curvature resumes, it is likely that we will have bought time, and decreased the likelihood of more serious interventions, because the remaining time for the progression of the curvature will be shorter until the patient reaches the end of bone growth. In the case series study referenced above, some of the patients who discontinued treatment, usually because they moved out of the area, did experience subsequent worsening of the curvatures, but the rib hump reductions persisted, so that these subjects had minimal rib cage distortion up through reaching bone maturity. If the study procedures have the expected value, there may be reduction in the number of unbraced subjects who require bracing, and the number of subjects who require spinal fusion surgery.

19.2 Indicate if there is no direct benefit
N/A

20. RECRUITMENT METHODS

20.1 Describe when, where, and how subjects will be recruited
Dr. Silva and colleagues will recruit the subjects from their regular patient population which includes 15-20 children and adolescents with scoliosis per week. The recruitment will take place in a private office during private communication between the doctor and the potential subjects and their parents/guardians. In both recruitment materials and consent materials, it will be made very clear that anyone who decides not to participate will not forfeit any future usual clinical services through Carrie Tingley Orthopedic Clinic. This should mitigate against undue influence during recruitment by the patient's clinical care provider. It should be remembered that Dr. Whyte Ferguson has an investment in establishing the usefulness of myofascial and articular care of AIS, but Dr. Silva and her colleagues have no investment in the outcome. For this reason, the recruitment, consent, and data collection and input into the REDCap system,(as well as data analysis) is appropriately shielded from any contact or influence by Dr. Whyte Ferguson.

20.2 Methods of identifying subjects
Dr. Silva and colleagues will be familiar with inclusion criteria (age 10 – 15, bone growth not yet complete, and x-rays showing Cobb angle of 15 to 30 degrees), and exclusion criteria (excluding curvatures that involve other diseases or conditions and are not strictly AIS). Children and adolescents with AIS are monitored every 6 months to decide what treatments they may require. The information that doctors will already be considering in this monitoring function include these same factors: age, size of curvature, and the type of curvature. The process of identifying subjects is simply an extension of their normal monitoring process.

20.3 Flyers or brochures that will be used to recruit subjects.
Flyers or brochures will be produced to recruit subjects and the recruitment brochure has been submitted as a document in our IRB submission.

21. PROVISIONS TO PROTECT THE PRIVACY INTERESTS OF SUBJECTS

21.1 Describe the steps that will be taken to protect subjects' privacy interests:
Data will be collected at the beginning and at the end of the research at Carrie Tingley. These data collection sessions will take a little more time than the usual every 6 month visit at Carrie Tingley, but otherwise the sessions are comparable. The privacy interests will be protected just the same way that privacy interests are already protected at Carrie Tingley. The data collected involves the same x-ray procedures that are currently in effect to monitor scoliosis patients every 6 months. Data collection will also include measurement of the rib hump performed by a nurse practitioner, and administration by the nurse practitioner of a Pain questionnaire and a Quality of Life questionnaire. The subjects will be informed about this data collection in the consent document. The rib hump measurements and questionnaire responses will be identified via a code for each respondent and will be entered into the REDCap system and will be de-identified. Once the statistician has correlated these responses for each subject, the data will thereafter be dealt with in aggregate terms for the purpose of statistical analysis.

The treatment sessions will be performed at CTSC clinical rooms or at Dr. Whyte Ferguson's private chiropractic office twice per month for 6 months, and the records of these visits will be kept confidential. The subjects' access to these office sites will be no different from the access of any member of the public to these sites. There is therefore no specific privacy risk associated with their coming and going from the treatment sites.

21.2 Describe the steps that will be taken to protect subjects' privacy including privacy protections during recruitment, consent, and data collection.
The protections of privacy in the process of recruitment, and data collection have already been described. The protections in the process of consent are discussed below in section 25.

22. ECONOMIC BURDEN TO SUBJECTS

22.1 Costs that subjects may be responsible for because of participation in the research.

RESEARCH Procedures	#	Responsible Party
For All subjects (Control and active treatment Cohorts):		
Measurement of Rib Hump	2	Study will cover expense
Questionnaire re Quality of Life	2	Study will cover expense
Questionnaire re Pain Level	2	Study will cover expense
For Active treatment subjects:		
Treatment sessions	12	Study will cover expense
Over the door chin up bar	1	Study will cover expense
Small ball for rib mobilization	1	Study will cover expense
Heel lift (if necessary)	1	Study will cover expense
Arch supports (if necessary)	1	Study will cover expense
Ischial Lift (if necessary)	1	Study will cover expense

STANDARD OF CARE Procedures	#	Responsible Party
All subjects		
No x-rays are performed as a part of this study, but we require the data drawn from x-rays:		
(pre and post x-rays)		
X-rays, Scoliosis Study	2	Participant or 3rd Party

22.2 Any other costs not already described

N/A Subjects' parents will be encouraged to supply their children with supportive footwear in which to place the arch supports. This footwear is not a requirement for participation in the study.

While performing partial hanging from a bar in a doorway, subjects will need to have their feet on the floor. If they are too short, parents will need to provide a suitable safe surface on the floor in the doorway, so that the partial hanging can be safely performed. It is not expected that this requirement, to provide a safe surface, will pose a financial burden.

22.3 Indicate whether subjects will be charged for investigational drugs, devices, procedures.

There will be no charge for procedures (or devices used as part of intervention protocol as listed above)

22.4 Explain who will be responsible for paying for treatment of adverse events

Due to the modest nature of the risk of procedures, muscle soreness that lasts 24 to 48 hours, no significant adverse events that would involve costs are expected. In other words, the possible treatment reaction is self limiting and does not require care.

22.5 Ensure that the cost section of the consent form reflects the costs that are covered by the sponsor and the costs for which the subjects (or 3rd party payers) are responsible.

Delineation of costs is included in the consent document.

23. COMPENSATION

23.1 Plans for Compensation

Reasonable compensation or reimbursement for subjects: Control group: $50 for control subjects to complete both the initial and 6 month evaluations: total compensation of $50/subject. Compensation will be made in the form of merchandise cards. Travel will not be reimbursed because these visits would have been expected anyway.

Active treatment group: $100 for completing each 3 months of treatments including the initial and final (6 month) evaluations: Total $200/subject. These compensations will be paid in merchandise cards. Travel reimbursement at the rate of $.20 per mile will apply to travel to all of the treatment sessions. (Twenty cents per mile is the amount set by the IRS for medical deductions for medical travel.) Travel to the initial and 6 month evaluation sessions at Carrie Tingley will not be reimbursed, because these sessions are already part of the usual care and monitoring of scoliosis patients.

24. COMPENSATION FOR RESEARCH-RELATED INJURY

24.1 Compensation if research involves more than Minimal Risk

Because the modest risk is self limited, 24 to 48 hours of increased muscle soreness, it is not expected that there will be any need for subjects to seek care associated with treatment procedures.

24.2 Subjects responsible for seeking their own care for research-related injury

Again, it is not expected that research subjects will need to seek medical care for anything they experience as a result of the treatment procedures. The maximum reaction to care that is anticipated in a portion of subjects is self limited muscle soreness of 24 to 48 hours duration. Subjects are encouraged to seek medical care from Dr. Silva or her colleagues, because she is providing medical oversight for this research project.

25. CONSENT PROCESS

25.1 Indicate whether you will be obtaining consent, and if so describe:

Dr. Silva with some help from colleagues will be obtaining consent for participation in this research study as part of the recruitment process. Waiver of consent and HIPAA Authorization is requested for screening and recruitment.

25.1.2 Where will the consent process take place and provisions for privacy

The consent process will take place at Carrie Tingley in a private office.

25.1.3 Steps to minimize possibility of coercion or undue influence.

Dr. Silva is a professional who is skilled in the consent process. Furthermore, there are sufficient numbers of expected eligible subject so this will minimize the likelihood of any pressure being placed on any individual subject or his/her family. Furthermore, Dr. Silva is

not the designer of the intervention and therefore does not have a stake, financial or otherwise, in whether or not sufficient subjects can be recruited.

25.1.4 Waiting period available between reviewing the study and consent information and obtaining consent.
The potential subjects and their parent/guardian will be encouraged to take whatever time they need to consider and execute the consent document and assent documents. If they do not decide by the time of their regular 6 month x-ray (the baseline measurement) or any follow-up visit for discussion of x-ray results, then a separate visit would be required to administer the other baseline questionnaires and the rib deformity measurement.

25.1.5 Processes to ensure ongoing consent throughout the study
It will be made clear to the participants that they can withdraw from the study at any time. Any concerns among those participating in the active treatment will be discussed and hopefully dealt with so that the subjects can successfully continue. It should be noted that participants and their parent/guardian are usually very eager to continue with any intervention that might possibly afford any help in managing AIS.

25.1.6 Steps that will be taken to enhance understanding
Dr. Silva understands that the consent process is not just a matter of presenting written consent documents and seeking signature. A discussion with each potential subject and his/her parent/guardian will take place that will include teachback or other forms of query to assure that they have understood the consent document.

25.1.7 Any procedure/testing for ensuring that the consent is understood by the potential subject
See previous answer.

25.1.8 Subjects not fluent in English: Indicate what language(s) other than English are understood by prospective subjects or representatives.
Spanish is the other language that may be spoken by subjects and their parents or guardians.

25.1.9 Translation
The study description in flyer or brochure will be translated into Spanish and the consent and assent documents will also be translated into Spanish, once the English versions have been accepted under the IRB process.

25.1.10 Short form consent documents
N/A

25.1.11-25.1.20 Consent for impaired adults
Apply to adults who are impaired and thus unable to consent. N/A.

25.1.21 Subjects who are not yet adults (infants, children, teenagers):
Age range of the children anticipated to be enrolled in the research: Ages 10 to 15.

25.1.22 Determining whether subjects have attained legal age of consent
N/A All subjects will be between 10 and 15 so none will have attained the age of consent.

25.1.23 Parental permission
Consent will be sought from both parents because the research involves minor risk which is greater than minimal risk (and also potential benefit to the individual subjects).

25.1.24 Describe process for obtaining consent from guardian
Guardian who wishes to consent will need to bring proof of guardianship, or sign a legal document asserting legal guardianship.

25.1.25 Describe whether the children to be enrolled in the research should be capable of providing assent.
Children to be enrolled in the research, who will be 10 -15 years old, should be capable of providing assent.

25.1.26 Assent obtained from all, some, or none of subjects (children)
All of the research subjects, in both the active treatment group and the control group will be asked to provide assent.

25.1.27 Assent process and documentation, waiver of consent
Assent documents will be age-appropriate.
Waiver of Consent: Waiver of Consent and HIPAA Authorization is requested, for screening/recruitment purposes. Screening will take place prior to the regular consent process.

26. DOCUMENTATION OF CONSENT

26.1 Consent document will be used.
Consent form will be provided using the consent templates available from HRPO website. Editable Word document is attached. Page #s:

26.2 Tissue banking consent
N/A

26.3 Consent: verbal or online and documentation
N/A

27. STUDY TEST RESULTS/INCIDENTAL FINDINGS

27.1 Sharing results with subjects
All subjects will be informed of the measurements of their scoliosis curves on x-ray. Those in the active treatment group will also be informed of the interventionist's measurement of their rib humps, because this will be part of the interventionist's ongoing monitoring of the

intervention process. Those in the active and control groups will also be informed about the aggregate results of the study.

27.2 Incidental findings

Incidental findings may present themselves as a result of x-ray examinations. Any incidental findings will be addressed in accordance with Carrie Tingley standard of care in the same manner as would be done for any patient. Information regarding how incidental findings will be handled will be addressed with patients within the consent document.

28. SHARING STUDY PROGRESS OR RESULTS WITH SUBJECTS

28.1 Subjects to be provided with progress report while study underway?

Subjects will not be provided with a summary of the trial progress, because there will only be baseline assessments and assessments at the end of the study.

28.2 Subjects to be provided with study results after study is complete?

Subjects will be provided with a summary of the study results at the end of the study period. Subjects already know whether they were assigned to the active treatment group or the control group. The mechanism for reporting will be an end-of study lay report summarizing results of treatment group as compared to controls. This report will be provided to subjects via mail, email, or in person per participants' request.

29. INCLUSION OF VULNERABLE POPULATIONS

29.1.1-29.1.7 and 29.1.9: This study does not include these vulnerable populations

N/A

29.1.8 Research involves children as subjects

The research involves individuals considered vulnerable: children aged 10-15 years old. The participation of patients in this age range is necessary and warranted given this study is designed to evaluate scoliosis, a condition specifically affecting children and adolescents during the developmental period. It is in this age range that maximal progression of scoliosis occurs and therefore the key period for intervention to alter the health outcomes.
Additional safeguards that will be put in place to protect the rights and welfare of these child participants include: (1) An age-appropriate description of the study including all test procedures, treatment visits, home exercises, follow-up testing and assessments will be provided in the assent documents to study participants and in consent documents to the parent/guardian, for their signatures. (2) These documents will be reviewed and discussed in person with the child participant, parent/guardian and clinician at the beginning of the study to assure understanding and answer any questions or concerns.

30. COMMUNITY-BASED PARTICIPATORY RESEARCH

30.1 Community involvement in design and conduct of research

This research does not include a community-based participation component. All subjects will be recruited from the Carrie Tingley pediatric patient population.

31. RESEARCH INVOLVING AMERICAN INDIAN/NATIVE POPULATIONS

31.1 Sensitivity to American Indian/Native Populations

While Native populations are not specifically a target for this study, they are eligible for enrollment and may become study participants. The proposed research is both acceptable and sensitive to local Native community attitudes as evidenced by results of the past published case series on these methods by the co-investigator which included this population (Whyte Ferguson L, 2017). Co-investigator's experience identified that the manual treatment modalities being studied, then and now, are highly compatible with tribal attitudes which can tend to prefer manual treatment over more invasive interventions. (Note that the co-investigator and designer of the AIS treatment intervention donated her time to provide care to Taos Pueblo members at the Pueblo 1-2 days per month, for 22 years.)

32. TRANSNATIONAL RESEARCH

N/A

33. DRUGS OR DEVICES

33.1-33.4: N/A

Research involves no drugs or medical devices. Treatment tools that may be used during an exam as part of the active protocol include (1) activator adjusting instrument (a low amplitude impulse device designed to facilitate spinal adjustments), (2) standard reflex hammer, (3) hydrocollators (moist heat packs). Treatment tools will be utilized, cleaned and handled in accordance with standard hygiene practices. Home tools that will be distributed to participants to use as part of the home exercise program include (1) small therapy ball (used in the supine position to act as a fulcrum enhancing extension at the rib-spinal juncture), (2) standard over-the-doorway chin-up bar to perform over-the-door stabilized stretching (feet on the ground). When appropriate, additional home devices may include heel lifts and arch supports, as well as ischial lifts, to balance the effects of any structural asymmetries and over-pronation.

These devices and tools are not the subjects of the research protocol but are commonly used tools within the chiropractic profession.

1. Principal Investigator's Assurance

By submitting this study in the Click IRB system, the principal investigator of this study confirms that:

X The information supplied in this form and attachments are complete and correct.

X The PI has read the Investigator's Manual and will conduct this research in accordance with these requirements.

X Data will be collected, maintained and archived or destroyed per HSC Data Security Best Practices, including:

1. **Best Practice for data collection** is for it to be directly entered onto a data collection form that is in a secured access folder on an HS drive behind a firewall, or in a secure UNM Data Security approved system such as RedCap.
2. **Data collection of <u>de-identified data</u>**, if done in a clinical setting or other setting that does not allow direct entry into a secured system, may be done temporarily using a personal or university owned electronic storage device or hard copy document. **The important security safeguard is that no identifiers be include if the data is entered or stored using an untrusted device or storage.**
3. **Permanent (during data analysis, after study closure**) storage must reside on HSC central IT managed storage. Processing of data (aggregation, etc.) are to be carried out in such a way as to avoid creating/retaining files on untrusted storage devices/computers. Trusted devices are HSC managed and provide one or more of following safeguards: access logs, encryption keys, backups, business continuity and disaster recovery capabilities.
4. **Alternate storage media** must be approve by HSC IT Security as meeting or exceeding HSC central IT provided security safeguards.

CHECKLIST SECTION

This section contains checklists to provide information on a variety of topics that require special determinations by the IRB. Please complete all checklists relevant to your research.

2. Partial Waiver of Consent for Screening/Recruitment

Complete this checklist if you are requesting a partial waiver of consent so that you can review private information to identify potential subjects and/or determine eligibility prior to approaching potential subjects for consent or parental permission.

A. Describe the data source that you need to review (e.g., medical records):

Medical records will be consulted to identify potential subjects.

B. Describe the purpose for the review (e.g., screening):

Medical records will be consulted for screening purposes.

C. Describe who will conducting the reviews (e.g., investigators, research staff):

Principal Investigator and her medical colleague will be consulting the medical record for screening purposes.

D. Do all persons who will be conducting the reviews already have permitted access to the data source?

X Yes

☐ No. Explain:

i. Verify that each of the following are true or provide an alternate justification for the underlined regulatory criteria:

1. The activity involves no more than minimal risk to the subjects because the records review itself is non-invasive and the results of the records review will not be used for any purposes other than those described above.

X True

☐ Other justification:

2. The waiver or alteration will not adversely affect the rights and welfare of the subjects because eligible subjects will be approached for consent to participate in the research and are free to decline. Further, the information accessed during the records review will not be disclosed to anyone without a legitimate purpose (e.g., verification of eligibility).

X True

☐ Other justification:

3. The research could not practicably be carried out without the waiver or alteration because there is no other reasonably efficient and effective way to identify who to approach for possible participation in the research.

   X True

   ☐ Other justification:

4. Whenever appropriate, potentially eligible subjects will be presented with information about the research and asked to consider participation. *(Regulatory criteria: Whenever appropriate, the subjects will be provided with additional pertinent information after participation.)*

   X True

   ☐ Other justification:

3. Partial Waiver of HIPAA Authorization for Screening/Recruitment

Complete the following additional questions/attestations if the records you will review to identify potential subjects and/or determine eligibility include Protected Health Information (PHI).

A. Will you be recording any PHI when conducting the records review to identify potential subjects and/or determine eligibility?

X Yes. Describe: The PHI will be accessed, including age, degree of curvature, and type of scoliosis, and then the subject will be assigned a code if the potential subject becomes an actual subject. The PHI of anyone who does not become a subject will be discarded or otherwise not retained.

☐ No

B. If you answered "Yes" to question 6 above, please describe when you will destroy identifiers (must be the earliest opportunity consistent with the conduct of the research) or provide justification for why they must be retained:

The coding and its correlation to the PHI will be retained only long enough for conduct of the research and statistical analysis and then the data will be used in aggregate form thereafter. The coding key will be destroyed at that time unless the coding key will be necessary for preserving data until subjects reach age 22.

C. The PHI accessed or recorded for identification/screening purposes will not be reused or disclosed to (shared with) any other person or entity, except as required by law, for authorized oversight of the research study, or for other research for which the use or disclosure of the PHI would be permitted under the Privacy Rule.

X True

☐ False

44. VULNERABLE POPULATIONS

A. Children

Complete this checklist if the subject population will include children.

1. Select the category of research that you believe this research falls within and provide justification for any associated criteria. If there are different assessments for different groups of children or arms (e.g., placebo vs. drug), include a memo to provide an assessment for each group.

☐ Research not involving greater than minimal risk. *(Minimal risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.)*

☒ Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects.

Provide justification for each of the following criteria:

(1) The risk is justified by the anticipated benefit to the subjects: because of the modest nature of the risk: self limited muscle soreness that may last 24 to 48 hours, any benefit that they may gain from the treatment regimen such as reduced pain, reduction of the size of the rib cage elevation or deformity, and/or reduction in the actual degrees of the curvature or reduction in the rate of increase of the spinal curvature would far outweigh the modest risk.

(2) The relation of the anticipated benefit to the risk is at least as favorable to the subjects as that presented by available alternative approaches: There can also be modest muscle soreness or skin breakdown associated with the use of spinal bracing or physical therapy exercises and procedures, thus the intervention is comparable to other available treatment approaches.

☐ Research involving greater than minimal risk and no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject's disorder or condition.

Provide justification for each of the following criteria:

(1) The risk represents a minor increase over minimal risk:

(2) The intervention or procedure presents experiences to subjects that are reasonably comensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational situations:

Yes

(3) The intervention or procedure is likely to yield generalizable knowledge about the subjects' disorder or condition which is of vital importance for the understanding or amelioration of the subjects' disorder or condition

Yes

☐ http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM126418.pdf

4. Data Transfer/Sharing (Checklist)

Complete this checklist if the research involves transferring/sharing of data with an external entity (institution, company, etc.).

A. Will data be transferred/shared with an external entity (institution, company, etc.)?

☐ Yes

X No. **The remainder of this section does not apply.**

B. Indicate if the data is incoming and/or outgoing:
C. Provide the name of the entity that data will be transferred/shared with:
D. Provide the contact name, email and phone number with whom data is being transferred/shared with:
E. Who is responsible for transmission of the data?
F. Who is responsible for receiving the data?
G. Describe how the data will be transferred/shared. Please note data cannot be transferred/shared without assistance from UNM HSC IT. **Requesting HSC Central IT Transfer is detailed on the Sponsored Projects website:**
H. For data being transferred/shared with outside locations or entities, describe the following:

- Where is data storage and how will it be maintained in a secure manner (i.e. encryption, password protection, use of Qualtrics or REDCap, etc)?
- What is method in which data will be collected and stored (i.e. electronic, hard copy, etc)?
- How long will the data be stored?
- Who will have access to data?

I. Please list all specific data elements, variables, etc. to be sent out and/or received. Indicate if the data contains identifiers and health information. Please note that identifiers that MUST be removed to make health information de-identified are as follows: Names, All geographic subdivision smaller than a State, All elements of year (except year),

Telephone, Fax numbers, E-mail addresses, Social Security, Medical record number, Health plan beneficiary, Account numbers, Certificate/license numbers, Vehicle identifiers and serial numbers, Device identifiers and serial numbers, Web URLs, IP address numbers, Biometric identifiers, full face photographic images, and Any other unique identifying number, characteristic or code.)

J. If the research requires the access, use, or disclosure of any of the 18 individually identifiable protected health information (PHI) identifiers that can be used to identify, contact, or locate a person (e.g., name, medical record number, etc.), are the subjects going to consent to or authorize the disclosure of their individually identifiable health information?
    a. ***Or*** is HIPAA authorization altered or waived?
K. What is the classification of the data (de-identified, limited data set, protected health information, other).
L. Does the request to transfer/share data include clinical data that belongs to the UNM Health Systems?
M. Does the data to be transferred/shared include information about patients seen at external health system or at a third party medical provider?
N. Is the external entity a "covered entity"?
O. Is the data that is going to be transferred/shared owned or partially owned by another party or have any type of restrictions including regulatory restrictions (i.e. HIPAA, FERPA, etc.)?
P. Is the data publically available? If yes, please provide details:
Q. Does the data include information about substance abuse treatment, sexually transmitted diseases, genetic testing results, HIV/AIDS testing results, and/or mental health?

5. Specimen Transfer/Sharing (Checklist)

Complete this checklist if the research involves transferring/sharing of specimens with an external entity (institution, company, etc.).

A. Will specimens be transferred/shared with an external entity (institution, company, etc.)?

☐ Yes

X No. **The remainder of this section does not apply.**

B. Indicate if the specimens are incoming and/or outgoing:

C. Provide the name of the entity that specimens will be being transferred/shared with:

D. Provide the contact name, email and phone number with whom specimens are being transferred/shared with:

E. Who is responsible for sending out the specimens? Please note specimens cannot be sent out without a fully executed material transfer agreement.

F. Who is responsible for receipt of the specimens? Please note specimens cannot be received without a fully executed material transfer agreement.

G. For specimens being transferred/shared with outside locations or entities, describe the following:

- *Where is specimen storage and how will it be maintained in a secure manner?*
- *What is method in which specimens will be collected and stored?*
- *How long will the specimens be stored?*
- *Who will have access to the specimens?*