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# A Retrospective CDSS Analysis to Compare Standardized and Non-Standardized Treatment for Central Sensitization Using Systemic Manual Therapy

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## Abstract

**Objective:** The purpose of this pilot study is to compare the efficacy and effectiveness of Systemic Manual Therapy (SMT) used in a pragmatic vs. standardized treatment strings across episode of care when treating patients with Central Sensitization (CS).

**Design:** Computerized Decision Support Software (CDSS) retrospective analysis of Electronic Medical Records (EMR) using the Halili Physical Therapy Statistical Analysis Tool (HPTSAT) to query EMR.

**Methods:** This study used the Halili Physical Therapy Statistical Analysis Tool (HPTSAT) to isolate two groups of sensitized patients, both treated with SMT but one using a pragmatic (XXXX) approach and the other a standardized one (BNUN). Paired and non-paired t tests were used to assess the differences in the reported Patient Identified Problem scale (PIP) across episode of care and between groups.

**Results:** The patients in both groups reported a statistically significant ($p < 0.001$) improvement across episode of care. The improvement in both groups (13.44 for the BNUN and 13.39 for the XXXX) was 3.5 times the MCID for the scale and above its 95% CI upper limit. There was no statistically significant difference in the rate of change between groups ($p = 0.98$)

**Discussion and conclusions:** This analysis demonstrated the efficacy of a standardized approach across an episode of care. These findings could become useful when treating patients with high complexity as well as a treatment arm in future RCT.

**Keywords:** Central sensitization, Systemic manual therapy, Temporal model for central sensitization

## Introduction

This research is a part of a larger multi-year investigation to understand the basis for Central Sensitization (CS), and the efficacy and effectiveness of Systemic Manual Therapy (SMT) in addressing it. The basis for this investigation is the Temporal Model for Central Sensitization (TMCS) [1] which proposes a functional mechanism explaining CS and its relationship and role in the development of neurodegenerative condition. The specifics of the TMCS are discussed in further detail toward the end of this introduction.

SMT [2,3], refers to a standardized physical therapy method that is based on several osteopathic approaches such as fascial counterstrain [4–10], visceral mobilization techniques developed by Jean Pier Barral [11], integrative manual therapy [12,13] and muscle energy techniques [14].

The key difference between how the techniques are performed in SMT and these original methods is that techniques are grouped into distinct set of protocols that are done in an exact order during a given treatment session. The protocol is referred to in the records using letter codes such as

"UD" or "DCS" etc. There are about 50 distinct SMT protocols and they are typically performed in a sequence of three to six protocols over several sessions with a specific therapeutic intent such as decongestion or desensitization. Several protocol sequences over an episode of care are referred to as a treatment string. Treatment sessions are typically done every seven to 14 days.

The fact that SMT is administered in a standardized manner paves the way for a quantitative evaluation of its efficacy and effectiveness, a feature not possible when using the source methods in their traditional manner. To date, there are several investigations to test and validate portions of the model [15–18].

One of the key observations in these studies was that there were several treatment sequences using SMT that appeared to be effective in treating CS. The purpose of this investigation is to compare the response to treatment using a standardized approach with these sequences and the response of the more common pragmatic treatment approach where the clinician chooses the protocols by applying other considerations.

Beyond the obvious interest in identifying an optimal string to treat CS over an episode of care, as evident by the following discussion about the TMCS, there is a yet unexplored relationship between CS and neurodegenerative conditions such as Alzheimer's (AD) and Parkinson's (PD) diseases. As such, there is an additional impetus to identify a standardized string of treatment that could be used as the treatment arm in a future randomized controlled trial (RTC) exploring this question.

## Theoretical framework

The TMCS includes three parts: the functional and structural circuitry of the Locus Coeruleus Noradrenaline system (LC-NA), the temporal elements of CS and their relationship to propagation of the condition, and the rationale behind the treatment approach using SMT.

The first part of the TMCS hypothesizes that sensitized state is preserved through tonic activation of the LC-NA system. The LC-NA system functions as a modulator of neurological functions such as sleep/awake cycles, attention, memory encoding and hormonal regulation [19]. During daily routine function, the system is active in a phasic mode creating subtle changes. However, when there is a perceived threat, the system shifts into a tonic activation mode causing activation of some neurological systems and inhibition of others [20]. The specific circuitry that is activated or inhibited depends on factors such as the trauma or threat response that created the initial potentiation and possible factors that modified that mapping. For example, a young infant might form a "freeze" response to facilitate hiding, an older child could potentiate a response that emphasizes fleeing from a person chasing them with a belt, and a young adult might form a more complex fawning response to deal with complex work or family situation [21].

While this response is generally self-abating and is not considered pathological, a sustained state of stress or multiple traumatic events can lead to propagation of this state. In accordance with the TMCS, this tonic activation mode is not fully sustainable leading to intermittent metabolic failure and dysregulation of the immune response [22]. As such, these dysfunctions could then propagate that tonic activation state via self-reinforcing neurologic and metabolic loops, erratic inflammatory response causing circulatory congestion and oxidative stress.

The second part of the TMCS is describing this system in functional temporal terms, dividing it into five levels. The first three levels represent the normal function of the LC-NA system, the fourth level represents the state of sensitization as described in the prior paragraph, and the fifth level accounts for a state of neurodegeneration.

At this fifth level, the model also suggests that in the presence of specific genetic mutations, and in the presence of sustained state of sensitization a neurodegenerative process can occur. There are likely multiple mechanisms in neurodegenerative failure can develop, but even if just some are consistent with this model, it is possible that treating CS can have a positive impact on some patients with neurodegenerative conditions.

Two plausible examples of this are described in the TMCS related to gene mutations associated with AD and PD. The following are the summary of the key points from this paper explaining these mechanisms.

One scenario that could lead to the development of AD is associated with a mutation of the α-secretase protein called disintegrin and metalloproteinase 10 (ADAM10). This protein is activated by acetylcholine (Ach), and it is necessary for the processing of amyloid precursor protein (APP) via a non-amyloid pathway.

When there is sufficient availability of α-secretase, the APP molecule will be processed to produce soluble amyloid precursor protein (sAPPα) which performs protective neuroregulatory functions. However, if α-secretase is scarce, the APP molecule will instead undergo cleavage by β-secretase and γ-secretase resulting in accumulation of amyloid beta (Aβ) as a byproduct [23–25] As Aβ accumulates, further accelerated neurodegeneration, that is independent of the prior metabolic sequelae, would take place [26].

In the previously discussed scenario, frequent tonic activation of the LC-NA causes reduced availability of ACh, which in turn causes reduction of overall availability of α-secretase (which is

already limited because a portion of it is in its nonfunctional mutated form, β-secretase.) The result is that the γ-secretase Aβ pathway becomes prominent.

This model can also be illustrated with individuals who carry the A53T mutation which causes over-production of alpha synuclein (α-Syn) leading to the development of PD. Overabundance of α-Syn has shown to limit the availability of the rate-limiting enzyme Tyrosine Hydroxylase (TH). TH is used in the conversion of L-Dopa to dopamine [27]. Under normal circumstances, when there is a limited availability of TH, dopamine is also produced (as a byproduct) by alternate enzymatic processes/pathways; these processes also generate reactive oxygen species (ROS) [28]. Those same enzymatic pathways are also used when there is oxidative stress created by increased demand for production of NA from dopamine [29].

As such, in the scenario where this secondary enzymatic pathway is already more prominent because of the overabundance of α-Syn because of the A53T mutation, is aggregated by the additional demand for dopamine as a precursor for norepinephrine created by tonic activation of the LC when CS is present, will cause the levels of ROS to rise beyond the self-regulatory capability of several superoxide dismutase (SOD) subtypes.

SOD normally converts ROS to other, less reactive agents [28], but with ROS rising to such high levels, the ROS start to bind with other structures such as α-Syn, provoking neurodegeneration [30,27]. As is the case with accumulation of Aβ in AD, the formation of Lewy bodies is likely to further escalate the cascade of destruction, independent of the original conditions leading to the production of ROS.

The third component of the TMCS focuses on the hypothetical treatment for CS using SMT. Since, as outlined in the first part of the model, the propagation of CS is attributed to tonic activation state via self-reinforcing neurologic and metabolic loops, erratic inflammatory response causing circulatory congestion and oxidative stress, the TMCS presents the hypothesis that an intermittent treatment over time to address these three elements using SMT should revert the LC-NA system back to functioning in a non-sensitized manner.

The model specifically theorizes that Barral GUOU and LAUG protocols can be used to disrupt the aberrant afferent visceral input attributed to the self-reinforcing loops. It also proposes that DCS and UD protocols should improve circulatory congestion and that CCCV would reduce oxidative stress.

Finally, the TMCS proposes a specific hypothesis testing scheme that can be used in future studies. This test requires the presence of three confounding conditions and one additional condition, that if met, would satisfy the requirement to reject the null hypothesis. The three confounding conditions include:

1. The study will have to demonstrate average improvement across episode of care in overall symptoms as well as in the specific problem studied.

2. At least one of the protocols associated with reduced afferent visceral input (Barral, LAUG, GUOU), one associated with reducing circulatory congestion (UD, DCS) and CCCV which associated with reduction of oxidative stress need to demonstrate efficacy better than the average care treating the specific problem studied (such as knee pain, for example).

3. The same protocols will also need to demonstrate the same efficacy in treating the patient's overall problems.

If all three of these conditions are met, the null can be rejected if the fourth condition, in which the protocols from the second condition that are not anatomically proximal to the area where the problem is studied, are still found to be more efficacious than the average care.

This hypothesis testing scheme was used successfully to reject the null in several studies: Aponte & Halili [15] found that in addition to meeting the three confounding conditions, both CCCV and DCS had passed the efficacy criteria despite the treatment area being anatomically remote from the lower back studied in this paper. Halili [16] had similar findings where both CCCV and DCS were efficacious in treating knee pain. To complete the picture, UD, BARRAL and LAUG have demonstrated a similar remote efficacy when treating chronic shoulder pain [18] and Jaw and facial pain [17].

In addition, these studies, as well as additional work [31–33] provided additional information that led to the incorporation of additional protocols into clinical practice to address congestion. These protocols are the basis for the lower and upper extremity decongestion sequences.

However, while providing important clinical and theoretical information, this work had not addressed the question of which specific string of SMT protocols and sequences produces the best clinical outcome addressing CS. **Table 1** lists the SMT protocols used in this study.

While the protocol letter coding system had been used for decades, the concept of a protocol sequence is more recent, and up to now, was never standardized. The clinical implementation of the concept of using treatment sequences was based on the validation studies [15–18] for the TMCS that in addition to validating the efficacy of the protocols proposed (UD DCS Barral LAUG CCCV GUOU), additional protocols had demonstrated a decongestive effect (LEDJ UEDJ VTCP CVVT). **Table 2** illustrates how clinically these two groups of protocols were divided into decongestive and desensitization sequences.

**Table 1.** Protocols.

| **List of SMT protocols with explanations [2,3]:** |
|---|
| **Barral (Barral abdominal motility):** This powerful protocol is a major player in desensitization sequences but also has a standalone benefit when treating visceral adhesions or pain. This protocol is often followed on the next session by CCCV protocol. This is done to stabilize certain side effects such as mood changes or to help shorten the relatively long adjustment process observed with some patients after the Barral protocol is used. |
| **CV (Cardio-Vascular):** CV is a short but powerful protocol. In addition to being part of several other protocols such as CVVT, CCCV and Barral-CV, it can have a powerful stabilization effect as a standalone protocol when patients are too sensitized to tolerate other interventions. |
| **CCCV (Cardio-Cervical-Cranial Vascular):** Facilitates sequential arterial dilation starting around the heart and progressing to the neck and brain arterial supply, enhancing the flow of oxygenated blood to regions in the brain that are metabolically stressed because of central sensitization. Often used the next treatment following Barral protocol to stabilize certain side effects such as mood changes or to help shorten the relatively long adjustment process observed with some patients after the Barral protocol is used. |
| **CVVT (Venous-Thoracic-Cardiovascular):** This protocol is a combination of techniques that focus on arterial and venous drainage, and is composed of two protocols, VT and CV. It is used to address respiratory issues and is a part of the upper extremity decongestion sequence. |
| **DCS (Diaphragm-Cranial-Sinus):** This protocol is one of the oldest protocols. It has gone through several minor modifications over the years but continues to be one of the more versatile protocols. It has a significant role in the desensitization sequence, but also seems to help with sinus headaches, migraines, certain types of vertigo, and normalization of parasympathetic function. The proposed mechanism for this protocol is facilitation of fascial release along the falx cerebri, falx cerebelli and the tentorium cerebelli, which are important dural folds that separate and support different sections of the brain. Additional components of this protocol primarily effectuate fascial release of several "transverse diaphragms" (this term is used to describe sites where transverse pressure is applied along the pelvis, the respiratory diaphragm, thoracic inlet, and the cranium.) These additional components were found to be necessary in many patients for the cranial portion of the DCS protocol to occur properly. |
| **GUOU (Gastro-Urinary-Ovarian-Uterine):** This protocol is a variation of the UD and GU protocols that has a more specific focus on reduction of congestion from the pelvis. As such it is useful as a standalone protocol for menstrual pain, hemorrhoids, HSV infections and other sources of pelvic pain. |
| **LAUG (Lower-Abdominal-Urogenital):** Fascial counterstrain-based protocol with focus on abdominal and pelvic organs. It is often used as part of a desensitization sequence or as the initial protocol in a lower extremity decongestive sequence. |
| **LEDJ (Lower Extremity Drainage Jones Version):** This is the main protocol for venous and lymph drainage from the leg and is used in the lower extremity decongestion protocol sequence. |
| MET SI (Muscle Energy Sacroiliac Joint): Designed to provide a consistent mechanical adjustment to the SI joint. |
| **RMG (Reverse Modified Glides):** This protocol is a combination of counterstrain nerve and venous techniques around the lumbar and thoracic spine. It stimulates movement of venous blood away from the spine to reduce congestion in that area. |
| **SIDJ (Sinus-Drainage-Jones Version):** This protocol is comprised of mainly fascial counterstrain and venous and lymph techniques. With this protocol, there is a moderate cranial and cervical drainage effect. |
| **SLMG (Side-Lying Modified Glides):** In this protocol the spinal nerve roots are mobilized by gliding the vertebral structures around them. This protocol is used as part of the lower extremity decongestive sequence and as a standalone protocol to address radicular pain. |
| **SPDJL (Spinal Ligament Jones Version Lumbar Area):** Addresses dysfunction associated with spinal ligaments and venous congestion in the middle to lower back area. It is used as part of the lower extremity decongestive sequence but when used alone can have the effect of inhibiting protective patterns that are manifesting as joint stiffness. |
| **SPDJC (Spinal Ligament Jones Version Cervical Area):** Addresses dysfunction associated with spinal ligaments in the cervical and upper thoracic area. It can be used as part of the upper extremity decongestive sequence but when used alone it can have the effect of inhibiting protective patterns that are manifesting as joint stiffness. |
| **SSMG (Speech and Swallow Modified Glides):** Combines treatment for anterior throat muscles with cervical modified nerve glides. This protocol can be used as part of upper extremity decongestive sequence (as an alternative to SLMGT) or as a stand-alone protocol to address cervical radicular symptoms. |
| **SYMPN (Sympathetic Nerve):** Contains a combination of sympathetic, parasympathetic, and vagus nerve branch techniques. It is often added at the end of a desensitization sequence (such as UD, DCS, Barral, CCCV, SYMPN) because it allows further stabilization of the autonomic nervous system by facilitating parasympathetic activity. |

**List of SMT protocols with explanations [2,3]:**

**UD (Urinary Drainage):** Found to be the most versatile protocol with contribution both to desensitization and decongestion. It has a consistent reproducible effect and is one of the few protocols that can be repeated several times in a row, with added improvement each time. While the exact mechanism of action is not entirely clear, the clinical effect is hypothesized to be created by manipulating autonomic control to various abdominal and visceral organs. Also, UD manipulates the circulatory system, instigating a "bladder tank" effect where for a brief period there is movement of fluid toward the extremities and then a reversal of direction of flow. This creates a powerful flushing effect.

**UEDJ (Upper Extremity Drainage Jones Version):** Uses fascial counterstrain and integrative manual therapy techniques to facilitate venous and lymph drainage from the upper limb. It is used as part of the upper extremity decongestive sequence but can be used as a standalone protocol to address acute injury to the arm or hand.

**VAS (Vascular):** Creates a strong flush effect around the lumbar spine. It is most effective when treating acute HNP (herniated nucleus pulposus) injury but is also effective in treating several spinal conditions that involve inflammation in that region.

**VASD UE (Vascular-Drainage Upper Extremity Version):** This is a standalone protocol that uses the VAS protocol as the base and adds two upper extremity techniques. This combination seems to utilize a reflex to activate drainage from the upper extremities via venous and lymph mechanisms.

**VTCP (Venous-Thoracic-Cardiopulmonary):** Has a moderate effect on the respiratory system and can be used as a standalone protocol to help with symptoms associated with respiratory issues such as asthma, COPD, pulmonary fibrosis, pneumonia or bronchitis. VTCP is often used (as an alternative to CVVT protocol) as the first protocol in the upper extremity decongestive sequence.

**Table 2.** Taxonomy of SMT protocol sequences.

| Sequence type letter | Variations | Protocol combinations included in category |
|---|---|---|
| **Desensitization sequences** | | |
| N | S: Short sequences | UD DCS Barral-CV CCCV<br>UD DCS LAUG CCCV<br>UD SIDJ GUOU CCCV |
| N | M: Medium sequences | Any combination of the short sequences with an additional protocol either in the middle, the beginning or end of a sequence. |
| N | L: Long sequences | Any combination of the short sequences with an additional two protocols either in the middle, the beginning or end of a sequence. |
| **Upper extremity decongestive sequences** | | |
| U | S: Short upper extremity decongestive sequences | VTCP UEDJ UD<br>CVVT UEDJ UD |
| U | M: Medium upper extremity decongestive sequences | Any combination of the short sequences with an additional protocol either in the middle, the beginning or end of a sequence |
| U | L: Long upper extremity decongestive sequences | Any combination of the short sequences with an additional two or more protocols either in the middle, the beginning or end of a sequence. |
| **Lower extremity decongestive sequences** | | |
| B | S: Short upper extremity decongestive sequences | LAUG LEDJ UD |
| B | M: Medium lower extremity decongestive sequences | Any combination of the short sequences with an additional up to two protocols either in the middle, the beginning or end of a sequence. |
| B | L: Long lower extremity decongestive sequences | Any combination of the short sequences with an additional of more than two protocols either in the middle, the beginning or end of a sequence. |
| **Decongestive sequence to the head** | | |
| H | M: All head decongestive sequences use an M as a second letter | CCCV DCS UD SIDJ<br>DCS CCCV UD DCS<br>Or any similar combination of these protocols |
| **Spinal focus sequences** | | |
| Y | M: All spinal focus sequences use an M as a second letter | Any combinations of protocol treating the back and spine such as METVAS, SLMG, SSMG, SPDJ or RMG |

### Research question

The specific research question for this investigation is if application of treatment in a standardized manner is comparable to treating patients with CS using a more common pragmatic approach. Based on the prior findings we hypothesize that this approach would have efficacy, but the comparison would help gain understanding of the degree of it.

## Methodology

It is a retrospective deidentified chart analysis using Computerized Decision Support Software (CDSS) modified from the HPTSAT [34] tool quarrying chart records from the Halilipt2022 EMR system for records between 04/02/2015 and 01/16/2026.

Over that period, treatment was provided by seven Physical Therapists (PT), four Physical Therapists Assistants (PTA) and number of physical therapy and physical therapy assistant students. Differences in treatment response between clinician groups (PT, PTA and students) were previously assessed [31] and no statistical differences were found between groups. As such, our confounding assumption for the purpose of this analysis is that treatment was provided in a technically uniformed manner.

### Outcome tool

The outcome scale used in this analysis is the Patient Identified Problem (PIP) scale [35]. This scale is used for each treatment visit and allows for a robust quantitative analysis. The PIP scale is a 1 to 10 scale with half point scoring allowed. The scale rates the severity of a given problem for the past week or so. A score of 1 denotes no problem (for a specific complaint on the list that was created in conference with the patient); 10 indicates the most severe problem.

A cumulative score of the whole scale is obtained by adding all the reported scores, dividing by the number of problems and multiplying by 10. To reduce bias, the patient's ratings are typically recorded before a therapy session regarding the prior week's treatment, instead of immediately after a therapy session. Also, when possible, the patient records the numbers on their own, using the computerized check-in system without receiving prompts from the therapist. During this process, the patient can see on the page the numbers that they reported last time to eliminate recall error issues. In occasional situations where a patient is not able to record their own numbers, the person recording the numbers for the patient is instructed to do so with as little prompting or suggestions as possible.

A validation study for the PIP scale [35] found the following: Construct validity was demonstrated by showing no significant change when no treatment was provided (avg change -0.59 (95% CI-1.8 to 0.6, $p = 0.34$) and significant change when treatment was provided (avg change 14.46, (12.57 to 16.35 $p < 0.0001$) a weak/moderate positive correlation with ODI, NDI, DASH, and LEFS ($r = 0.27, 0.41, 0.45, 0.30$ respectively) established a level of concurrent validity. Scale reliability was excellent (ICC = 0.96, 95% CI 0.93 to 0.97). Excellent responsiveness was demonstrated by AUC 0.78, +LR 7.55, -LR 0.39, specificity 91.46, and sensitivity 64.45. MCID for the full scale was determined to be 3.8 points (95% CI 1.4 to 8.2) and for individual score was 0.89 (95% CI 0.3 to 1.5).

Because the PIP scale enumerates and tracks cumulative score of all the patient's complaints, it has performed well as a surrogate to more specific CS outcome tools such as the Central Sensitization Inventory (CSI) [36]. The established MCID for the scale could be helpful as another metric when establishing differentiation between strings.

### Analysis process

After importing the deidentified chart data using the pre-established HPTSAT querying procedures, the study sample was created by isolating all patients identified as sensitized in their differential diagnosis by their treating physical therapists. In accordance with the facility guidelines, the determination of having CS is done using a methodology like the one outlined by Lluch et al. [37]. In these situations, the evaluating physical therapist would screen symptoms such as Widespread mechanical hyperalgesia and allodynia, thermal hyperalgesia, hypoesthesia and reduced vibration sense, dynamic measures of CS such as insomnia, anxiety, bowel or bladder dysfunction and other persistent symptoms of dysautonomia.

The length of episode to be studied was determined by looking at similar episode of care length: 15 [18], 20 [33], 16 [15], 18 [17], and 24 [16] yielding an average of 18 treatment per episode. This was done to minimize the internal validity threat of selection bias since patients being treated longer than the episode of care might be sicker than the average population studied.

In addition to having at least 18 treatments, the sample only included patients that did not have a treatment gap greater than 90 days to control maturation and history validity threats.

The final step in creating the study group was to have the HPTSAT query that isolated the final two groups for comparison. These groups included the patients that were treated using SMT protocols using a pragmatic not standardized approach and a group given a treatment using a lower extremity decongestive sequence followed by a desensitization sequence, an upper extremity decongestive sequence and culminates with a second desensitization sequence. The taxonomy used for the pragmatic treatment group was XXXX and for the standardized sequence group BNUN. The demographics of each group are listed in **Table 3**.

### Statistical analysis

Using MedCalc software (Version 23.4.1 MedCalc software Ltd 2025) a paired sample t test was done to evaluate the pre and post changes in the PIP scores of each group and a Welch's t test was done to compare the observed difference between groups.

## Results

From the total of 3,579 patients in the database, 1,991 met the criteria of suffering from CS by their evaluating physical therapists. Within that group, 533 had at least 18 uninterrupted treatment visits. From that group, 186 patients were excluded because their treatment string could not be allocated to either the BNUN or the XXXX groups. Exclusion from the BNUN group was done if the treatment string did not include a variant of the three types of sequences in the prescribed order. Exclusion from the XXXX group occurred when the treatment was comprised of a string of sequences (other than the BNUN order).

The remaining sample included 54 patients in the BNUN group and 293 in the XXXX group. **Table 3** includes additional demographic information about the samples.

**Table 4** summarizes the results of the paired and Welch's t tests.

Among the BNUN group, 87% (47) of the patients reported improvement while 13% (7) reported worsening symptoms at the end of 18 visits; among the XXXX group 78% (229) reported improvement over 18 visits, 3% (8) reported no change and 18% (53) reported worsening symptoms.

Both groups' PIP scores had improved throughout the episodes of care at a rate of 3.5 times the MCID of 3.8 for this scale. This rate was above the upper limit of the scale 95% CI of 8.2 points providing further indication that the improvement was clinically meaningful. There was virtually no difference ($p = 0.98$) in the rate of improvement between the groups.

## Discussion

The results of this study address the research question and hypothesis by demonstrating that both the pragmatic approach in the XXXX and the standardized sequence in the BNUN groups demonstrated similar efficacy and clinical value. In addition to suppressing the MCID the average improvement of 13.4 points and percentage of patients that improved in either group was better than the numbers demonstrated in prior studies [15–18].

It is possible that despite reaching similar rates, the improvement over episode of care occurred for different reasons in each group. In the pragmatic treatment group, the favorable outcomes could be attributed to a patient or impairment specific clinical decision-making process while the improvements in the standardized group could be due to the adherence to sequences that specifically targeted central sensitization. Clinical decision making, done by an experienced clinician, could prove to be helpful in targeting patient specific issues while the standardization approach efficacy is derived from its reliance on the treatment principles outlined in the TMCS and its accompanying validation studies.

If replicated in future studies, these findings could serve as the basis for using the standardized treatment when patients' complexity makes it difficult to identify the therapeutic target. In addition, since standardization is necessary in situations like RCT, this could provide the treatment arm for future study.

**Table 3.** Study demographics.

| Group | AVG Age | Min Age | Max Age | SD Age | Males | Females | Total |
|---|---|---|---|---|---|---|---|
| **BNUN** | 65.14815 | 25 | 88 | 14.53091 | 12 | 42 | 54 |
| **XXXX** | 61.34471 | 11 | 88 | 16.15106 | 70 | 224 | 293 |

**Table 4.** Results.

| Group | Start PIP | End PIP | Mean Change | SD | 95% CI | p (paired) |
|---|---|---|---|---|---|---|
| **BNUN** | 53.63 | 40.19 | 13.44 | 16.7509 | 18.02 to 8.87 | **<0.001** |
| **XXXX** | 56.93 | 43.54 | 13.39 | 17.1 | 15.37 to 11.42 | **<0.001** |
| **Difference (between groups)** | 3.3 | 3.35 | 0.05 | | | |
| **SD(Pooled)** | 15.03 | 18.19 | 17.04 | | | |
| **95% CI** | 7.69 to 1.1 | 8.66 to 1.95 | 5.02 to 4.92 | | | |
| **p (uneven sample)** | 0.14 | 0.21 | **0.98** | | | |

### Limitations

- The BNUN group, although standardized, lacks more specific information on the subtypes of the sequences such as length and other protocols used in addition to the core sequence protocols.
- Since the pragmatic group apparent reliance on the clinical decision-making process, the replicability of the outcome in other settings might vary.
- This type of investigation is not intended to confirm a specific physiological mechanism for the treatment protocols but rather to evaluate whether the hypothesis for the pathology and treatment is consistent with the results.
- The difference in group size between the groups could have caused the results to appear similar when they were not.
- The knowledge of the actual mechanisms of action of the SMT protocols is still evolving.
- The absence of randomization when selecting patients or protocols introduces bias, considering confounding variables such as differences in age, gender, duration of symptoms, or concurrent conditions were not adequately accounted for. This might limit the generalizability of the findings, making it difficult to conclude that the observed effects were due to SMT alone.

## Conclusions and Recommendations for Future Work

The results of this pilot study are consistent with prior work that supports the efficacy and effectiveness in treating sensitized patients with SMT. However, this is the first analysis that demonstrated the efficacy of a standardized approach across an episode of care. These findings could become useful when treating patients with high complexity as well as a treatment arm in future RCT.

Future work should further explore this concept and in addition to replicating the findings in a larger dataset look at additional questions such as optimal frequency, episode length, a more specific combinations.

## Ethics Statement

This study was previously examined and received an exempted status by Argus Independent Review Board (www.argusirb.com) on July 21, 2021.

## CRediT Author Statement

Dr. Halili contributed to this work with conceptual planning, design, writing and editing.

Mrs. Mischler contributed to this work with editing, revision, and conceptual elements.

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