

Complementary and Integrative Medicine for the Treatment of Tourette's Syndrome

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Abstract: Background: There is widespread interest in complementary and integrative medicine (CIM) among people with Tourette's syndrome (TS). Objective: To perform a systematic review of evidence on the use of CIM to reduce tics and improve tic-related quality of life. Methods: We included clinical studies of CIM in children, adolescents and adults with TS and chronic tic disorders, and assessed the change in tic severity and/or tic-related quality of life using validated scales. Risk of bias of randomized controlled trials was assessed using the risk of bias tool of the American Academy of Neurology, which classifies studies into Class I, II, III or IV based on quality criteria. Results: 49 clinical studies and three systematic reviews were included. Most studies were rated Class IV and therefore at high risk of bias. Class I studies demonstrated efficacy of functional MRI neurofeedback, 5-Ling granule, Jingxin Zhidong formula, and Ningdong granule in reducing tic severity. Class II studies suggest efficacy of mindfulness-based intervention for tics, acupuncture combined with atlantoaxial joint bone setting therapy, and art therapy. Systematic reviews summarizing the Chinese literature on acupuncture, acupuncture with herbal medicine and massage therapy suggest greater reduction in tics compared to conventional treatments but there is low confidence in the evidence due to poor methodological quality of included studies. Conclusions: Evidence to support the use of complementary and integrative medicine for TS is limited in methodological quality and widespread applicability. These limitations prohibit evidence-based recommendations for general use among individuals with TS.

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Tourette's syndrome (TS) is a common neurodevelopmental disorder characterized by the presence of multiple motor and at least one vocal tic, which are present for at least one year.¹ Tics characteristically begin in early childhood, peak in severity between 10 and 12 years of age and improve in adolescence. By the age of 16 years, nearly 80% of youth have either mild, minimal or no tics.² While children and their parents are often reassured by the favorable prognosis for tics in the long-run, tics can be impairing and cause emotional distress. Medications for tics can be helpful and have good evidence to support their use, but long-term treatment can be limited by adverse effects.³ Some parents are reluctant to treat their children with medication for tics and seek other options. There is good evidence to support the use of behavioral interventions,⁴ but as treatment must be provided by a trained professional, access is not universally available.

Complementary or alternative medicine refers to a broad set of health care approaches that are not typically part of or fully integrated with conventional medical care in each country, or that may have origins outside of “Western” medical practice. When non-mainstream approaches are used together with conventional medicine, it is considered “complementary.” Integrative medicine brings conventional and complementary approaches together in a coordinated way, bringing together multimodal interventions in various combinations to attempt to address the physical, emotional, social, spiritual and environmental factors that can affect a person's health and well-being. Kompoliti⁵ performed interviews with adults and caregivers receiving care for TS to assess the prevalence of complementary and alternative medicine use, factors influencing their use and efficacy as perceived by participants. One hundred participants completed the study, 76% of whom were male, at a mean age of 21.5 years. Complementary and alternative medicine use was reported in 64% of participants, with the most used modalities including prayer (28%), vitamins (21%), massage (19%) and dietary supplements (15%). Fifty-six percent of participants reported some improvement in tics. Eighty percent of users did not consult a doctor before starting treatment, and only 19% informed their doctor after starting.

Although there is frequent use among people with TS of complementary and integrative medicine (CIM) for tics, evidence to support their use in this population remains limited.

Objectives

This systematic review addresses the following questions:

1. In people with TS, does CIM reduce or improve tic severity and tic related quality of life compared to placebo or other treatment types?
2. In people with TS, does CIM cause adverse events compared to placebo or other treatment types?

Methods

A systematic review protocol was registered on the Open Science Framework (osf.io) prior to conducting the review.

Eligibility Criteria

Study Design

We included clinical studies of CIM for treatment of TS, including systematic reviews of clinical studies. We excluded single case reports.

Participants

We included studies with participants of any age with TS or other chronic tic disorders.

Interventions

We included all interventions characterized or defined as CIM. Interventions were classified into the following categories:

Mind–Body Practices.

Manipulation/Bodywork.

Supplements (natural products, dietary nutrients, vitamins, and minerals).

Traditional Chinese Medicine.

Other Integrative and Lifestyle Approaches.

Comparison Group

We included studies comparing CIM to placebo or other interventions, waitlist controls, and studies without a comparison group.

Outcome Measures

We assessed change in tic severity and/or change in tic-related quality of life using validated scales. Our preferred outcome scales were the Yale Global Tic Severity Scale (YGTSS) and the Gilles de la Tourette Syndrome Quality of Life Scale (GTS-QOL). Outcomes related to adverse effects included serious adverse events (death, hospitalization) and adverse event related treatment discontinuation.

Language

Studies published in English, French, Spanish, German, Italian and Polish were included in our review, due to the availability of study group members with fluency in these languages.

Publication Status

Only published articles were included.

Information Sources

We searched for studies meeting our inclusion criteria on OVID Medline, CENTRAL and PsycInfo.

Search Strategy

Please see Appendix A for our full search strategy for each database.

Study Records

Data Management

We used Covidence software to track our literature search and facilitate our systematic review. Covidence allowed us to simultaneously review abstracts, import full text articles and avoid duplication of work between independent reviewers.

Selection Process

Abstracts were reviewed in duplicate, with any discrepancies resolved by a third reviewer where applicable. All abstracts felt to be relevant proceeded to full text review (also in duplicate) for study eligibility based on our inclusion and exclusion criteria.

Data Collection Process

Study data were independently extracted by a single reviewer with accuracy confirmed by a second reviewer. Data were extracted for articles using predesigned data extraction forms.

Risk of Bias in Individual Studies

The risk of bias of randomized controlled trials (RCTs) was assessed using a risk of bias tool developed by the American Academy of Neurology. This tool classifies studies based on risk of bias into Class I, Class II, Class III, or Class IV.⁶

Reporting of Findings

Open-label studies and case series reporting the effect of interventions are considered Class IV studies. In the results section, we describe Class I, II, and III studies, and simply list Class IV studies as they are at very high risk of bias and do not drive evidence-based practice. All studies are summarized in Tables S1–S4.

Results

The initial database search was conducted on March 28, 2024. Forty-seven articles were included in the review: 44 clinical studies and three systematic reviews. See Figure 1 for PRISMA flow diagram. Immediately prior to manuscript submission (June 18, 2025), the search was re-executed, resulting in the addition of five clinical studies.

Mindbody Practices (See Table S1)

Biofeedback

Nagai performed a Class III RCT of biofeedback for tics⁷ in 21 participants randomized to active or sham biofeedback, attending three 30-min sessions weekly for 4 weeks. Both active and sham biofeedback participants experienced an improvement in tic severity, with no significant differences between groups.

Sukholdolsky performed a Class I RCT of real-time functional MRI neurofeedback for tics in adolescents with TS.⁸ The investigators tested if training participants to control the current average activity of the supplementary motor area using neurofeedback could help diminish tic severity. Twenty-one adolescents with TS participated in this crossover trial, with all participants completing both the neurofeedback and sham neurofeedback conditions. Analysis of the full dataset revealed a positive carryover effect with a significant treatment by sequence interaction. Analysis of first period data revealed a significantly greater improvement in tic severity on the YGTSS with neurofeedback compared to sham, with a mean difference of -3.8 (95% CI $-7.15, -0.40$). The authors however were unable to confirm that the treatment worked by the proposed mechanism of action – improved control of the supplementary motor area – based on assessment of their secondary outcome measures.

There are several Class IV studies of various biofeedback treatments, including using the galvanic skin response,⁹ EMG,¹⁰ EEG,¹¹ infra-low frequency neurofeedback¹² and neurofeedback with imagery training.¹³

Deep Breathing

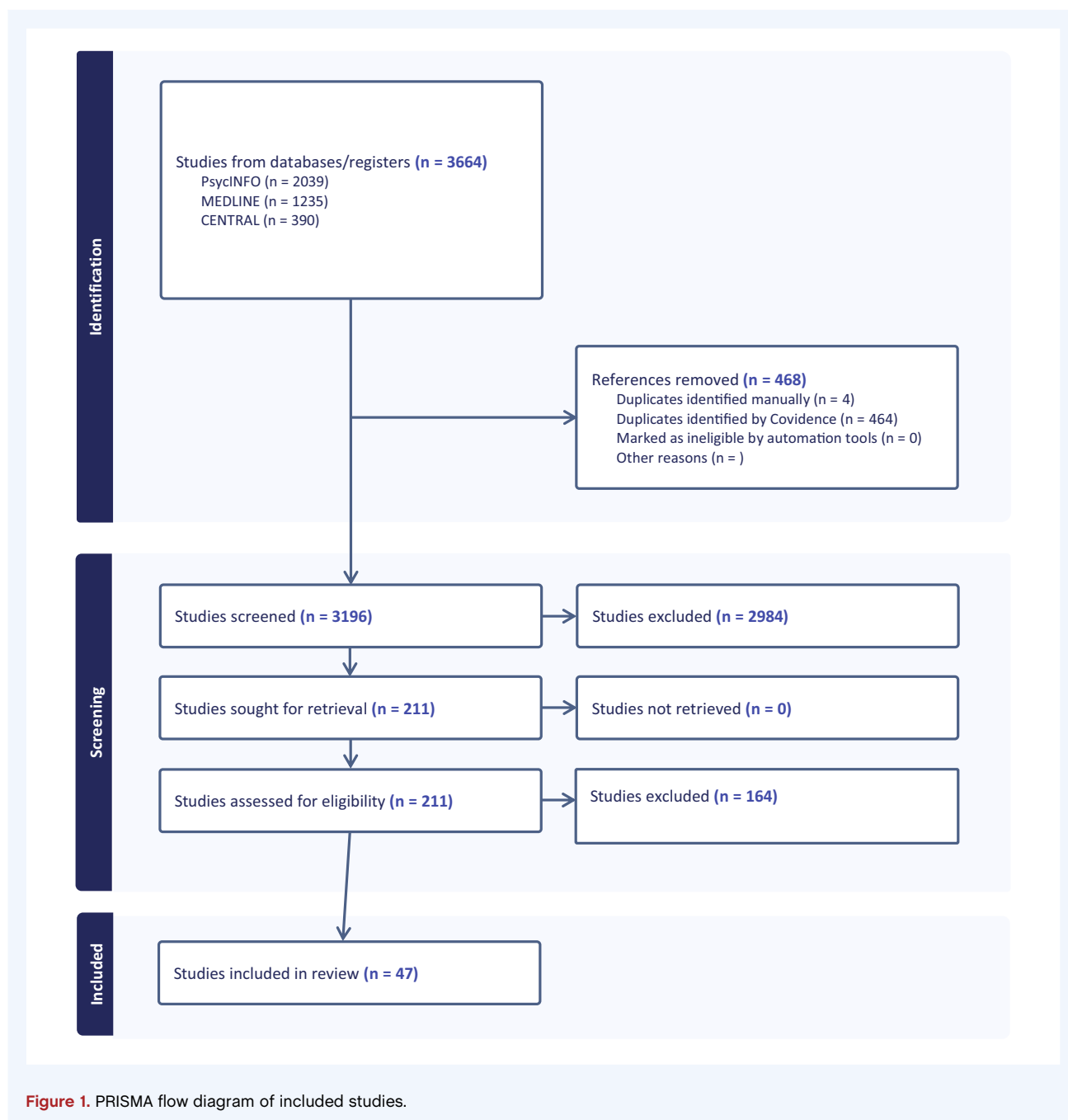
One Class IV study reported efficacy of instruction in deep slow nasal respiration in 10 adults with TS.¹⁴

Hypnosis

There are five Class IV studies of hypnotherapy in TS, consisting of case series.^{15–19}

Mindfulness

Reese conducted a Class II RCT comparing videoconference-delivered group mindfulness-based intervention for tics (MBIT) to videoconference-delivered group psychoeducation, relaxation and supportive therapy (PRST) in 32 adults.²⁰ Both groups received eight weekly 90-minute group treatment sessions and home practice. Participants receiving MBIT had significantly greater improvement in tic severity on the YGTSS than those receiving PRST, with a mean difference of -7.34 points (95% CI $-13.97, -0.72$). Tic-related impairment on the YGTSS was also significantly greater with MBIT, with a mean difference of -8.67 points (95% CI $-15.04, -2.3$). There are also two Class IV studies of mindfulness-based stress reduction for TS, one studying 18 youth and adults in an open trial,²¹ and one studying



five adults in an open trial of an online mindfulness-based group intervention.²²

Resource Activation

There is one Class IV study of resource activation for TS in an open study of 24 children and adolescents.²³ Resource activation in psychotherapy is defined as focusing on the resources, strengths and potential of the patients receiving the therapy and how they influence the therapeutic response.

Sensorimotor-Based Therapy

There is one Class IV study of the effect of sensorimotor strategies for the treatment of tics in an open label study of 10 children with TS and chronic tic disorders.²⁴

Relaxation Therapy

Bergin and colleagues performed a Class II RCT of relaxation training compared to a control intervention in children and adolescents with TS.²⁵ This study included 16 participants, with

seven receiving the intervention and nine receiving minimal treatment. The intervention consisted of six weekly 1 h training sessions on awareness, diaphragmatic breathing, behavioral and applied relaxation techniques, and biofeedback. The control group received the same number of visits, during which they listened to recordings of music or sounds and were asked to sit quietly. Several measures of tic severity were performed at baseline, after the six-week intervention period and at 3 months, including the Hopkins Motor and Vocal Tic Scale, the YGTSS, the Tourette Syndrome Severity Scale, the Parent Linear Analogue Scale and the Goetz Videotape Scale. At the end of the study, those receiving relaxation therapy demonstrated greater mastery of relaxation compared to participants in the minimal treatment group. Improvement in tic severity was noted in both groups at 6 weeks and 3 months, however there was no significant difference between groups (scale scores not provided in manuscript).

There are two Class IV studies of relaxation therapy, consisting of case series.^{26,27}

Manipulation/Bodywork

Acupuncture

We found two systematic reviews that summarize evidence on the use of acupuncture²⁸ and the use of acupuncture combined with herbal medicine²⁹ in children and adolescents with TS.

Lu²⁸ performed a systematic review and meta-analysis of RCTs of thin or fine solid needles into known acupuncture points or other specific body sites, including manual acupuncture, electroacupuncture, scalp acupuncture, auricular acupuncture, warm needling, navel acupuncture, thumbtack needling, plum-blossom needling, and intradermal needling. Eligible comparators included sham or placebo acupuncture, waitlist control, no treatment, or pharmaceutical treatment. They used the YGTSS total tic score or global score as the primary outcome and searched for studies published until April of 2020. Risk of bias was evaluated using the Cochrane Collaboration's bias risk assessment tool. They included a total of 22 studies with 1668 participants, all of which were reported in Chinese and conducted in China. Of the included studies, the most common intervention used was manual acupuncture (14 studies), followed by scalp acupuncture (five studies). Antipsychotics (haloperidol, thiorpride, tiapride, risperidone, aripiprazole) were the most common comparators, used in 19 studies. Most studies were rated at high risk of bias due to inadequate evidence of blinding of outcome assessors and participants, and at unclear risk for allocation concealment. Fifteen studies evaluated changes in YGTSS scores, with meta-analysis of these studies demonstrating a mean difference of -2.79 , 95% CI -4.75 , -0.82 , favoring acupuncture. When study data were sub analyzed by acupuncture type, there was a significant improvement relative to comparators for electroacupuncture only. A funnel plot showed an asymmetrical distribution, suggesting publication bias. Lue discussed that in traditional Chinese medicine, it is generally believed that tic disorders are due to an excess of yang and a deficiency of yin, with

the liver being the key organ involved in pathogenesis. Most included studies used acupoints focusing on regulating the mind and calming the liver. Limitations of included studies were generally poor methodological quality and small sample sizes.

Li²⁹ performed a systematic review and meta-analysis of RCTs of acupuncture combined with herbal medicine, compared to Western medicine. Studies that included participants with psychiatric comorbidities were excluded. An assessment of risk of bias was performed using the Risk of Bias Tool 2.0, and studies published up to November 2022 were included. Eighteen studies met inclusion criteria, with a total of 1400 participants. All experimental groups were treated with acupuncture plus herbal medicine, while Western medicine comparators included tiapride in 14 studies and haloperidol in four studies. All studies were rated at high risk of bias due to inadequate evidence of blinding and allocation concealment. Eleven of the studies reported the YGTSS total score as an outcome measure, with meta-analysis of studies revealing a mean difference of -3.91 , 95% CI -5.49 , -2.33 , favoring acupuncture combined with herbal medicine. Evidence of publication bias was present, with an asymmetry on the funnel plot and a positive Egger's test. Li states that the pathogenesis of TS relates to yin deficiency and yang excess. The use of acupuncture points and herbal medicine attempts to restore normal function by balancing yin and yang. Mentioned limitations of the systematic review include the low quality of included studies and their small sample sizes, as well as publication bias.

Acupuncture Combined with Bone-Setting Therapy

Lang³⁰ performed a three-arm Class II RCT comparing acupuncture combined with atlantoaxial joint bone setting therapy to acupuncture alone and tiapride (50–200 mg BID) alone. Six hundred children and adolescents with TS participated in the trial and were randomized equally to each of the three arms for 2 months. The frequency of acupuncture and bone setting therapy was not specified. Participants receiving acupuncture and atlantoaxial joint bone setting experienced greater improvement in the YGTSS total tic severity score compared to acupuncture alone, RMD -2 (95% CI -3.4 , -0.6), and compared to tiapride, RMD -4 (95% CI -5.4 , -2.6). Participants receiving acupuncture alone also had significantly greater improvement than those receiving tiapride, with a RMD -2 (-3.4 , -0.6).

Massage Therapy

Wu and colleagues³¹ performed a systematic review and meta-analysis of RCTs of pediatric massage therapy for the treatment of tic disorders in children. As described in their review, massage therapy is rooted in Chinese medicine and uses techniques to stimulate body acupuncture points and meridians for therapeutic purposes. They found 19 studies all published in Chinese and conducted in China, including a total of 1423 participants. In these studies, the control group was given conventional drug

therapy (including aripiprazole, haloperidol, thiorpride hydrochloride, herbal medicines or tonics, or Chinese medicine), and the experimental group was given massage therapy alone (16 studies) or combined with conventional drug therapy (three studies). The included studies had overall low methodological quality, with most studies not providing adequate reporting on randomization, allocation concealment, or blinding. Twelve studies reported YGTSS scores as an outcome, including 854 participants. The raw mean difference between control and massage therapy was -2.42 points, 95% CI $-3.97, -0.88$, favoring massage therapy. Begg and Egger tests showed no evidence of publication bias. The authors concluded that pediatric massage therapy alone or in combination with conventional treatment was superior to conventional treatment alone in improving symptoms in pediatric tic disorders. Limitations of the review expressed by the authors include that since all included studies were conducted in China, the results might not be applicable to non-Chinese populations, and that the low methodological quality of included studies undermines the reliability of the evidence.

Supplements (See Table S2)

Omega-3 Fatty Acids

Gabbay performed a Class II RCT of omega-3 fatty acids in 33 children and adolescents with TS.³² Participants were 6 to 18 years of age, meeting diagnostic criteria for TS. Participants were randomized to 500–1000 mg of omega-3 fatty acid or placebo for 20 weeks. The study failed to achieve its primary outcome, which was a 30% reduction in the YGTSS total tic score compared to baseline. A higher proportion of participants receiving omega-3 fatty acids had a greater than 30% reduction in the Impairment score on the YGTSS, 59% vs. 25%, $p < 0.05$.

Vitamin D

There is one Class IV RCT comparing high-dose versus low-dose vitamin D3 supplementation in 83 children with chronic tic disorders.³³

L-Theanine and Vitamin B6

There is one Class IV RCT comparing L-Theanine 200 mg/day and Vitamin B6 2.8 mg/day versus weekly psychoeducation in 34 children and adolescents with TS or chronic tic disorder.³⁴

Lactobacillus Plantarum PS128

There is one Class I RCT of PS128, a probiotic (*Lactobacillus plantarum*), versus placebo in 58 children and adolescents with TS.³⁵ Children were randomized to treatment for 8 weeks, with tic severity on the YGTSS serving as the primary outcome. There was no significant difference between PS128 and placebo in the change in the YGTSS total tic score from baseline, with an RMD of 1.13, 95% CI $(-1.76, 4.02)$.

Limosilactobacillus Reuteri

There is one Class IV RCT comparing limosilactobacillus reuteri to clonidine transdermal patch in 57 children with TS.³⁶

N-Acetylcysteine

There is one Class I study of N-acetylcysteine in children and adolescents with TS or chronic tic disorder.³⁷ Thirty-one participants were randomized to N-acetylcysteine 2400 mg/day or placebo for 12 weeks, with the YGTSS total tic score the primary outcome. There was no significant difference between N-acetylcysteine and placebo in improving tic severity on the YGTSS, with a mean difference 3.0 (95%CI $-1.46, 7.46$). There were no differences in side effect rates between N-acetylcysteine and placebo, and no severe side effects reported.

Magnesium and Vitamin B6

There is one Class IV open label study of magnesium and vitamin B6 for tics in 10 children and adolescents with TS.³⁸

Traditional Chinese Medicine (See Table S3)

There is one Class I RCT of 5-Ling Granule for the treatment of tics in children and adolescents with TS and a condition fitting the excessive subtype based on traditional Chinese medicine-based diagnosis.³⁹ Participants were randomized to 5-Ling Granule ($n = 363$), placebo ($n = 117$), or tiapride ($n = 123$) for 8 weeks, with the YGTSS total tic and impairment scores serving as the primary outcomes. There was a significantly greater improvement on the YGTSS total tic score at 8 weeks with 5-Ling Granule compared to placebo, with a mean difference of -3.8 points (95% CI $-5.3, -2.3$). There was no difference between 5-Ling Granule and tiapride, with a mean difference of 0.5 points (95% CI $-0.83, 1.83$). Impairment on the YGTSS was also significantly greater with the 5-Ling Granule than placebo, with a mean difference of -5.6 points (95% CI $-7.6, -3.7$), and no difference between 5-Ling Granule and tiapride (0.4, 95% CI $-1.3, 2.1$). There is also a Class II RCT of 5-Ling Granule, under the name of shaoma zhijing granules, that contains identical ingredients to the previous study.⁴⁰ In this study, 80 children and adolescents with tic disorders and meeting traditional Chinese medicine diagnostic criteria for hyperactive liver wind syndrome were randomized to shaoma zhijing granules or tiapride for 8 weeks. There was no difference at endpoint in the YGTSS total tic score between treatment groups, with a RMD of -1.25 (95% CI $-5.08, 2.58$).

There is one Class I RCT of Yi-Gan-san for the treatment of tics in children and adolescents with TS.⁴¹ Participants were randomized to Yi-Gan-san ($n = 19$) or placebo ($n = 19$) for 4 weeks, with the YGTSS Global Score serving as the primary outcome. There was no difference after 4 weeks of treatment between groups, with a mean difference of 3.33 points (95% CI $-11.06, 17.72$) on the YGTSS Global Score.

There is one Class I RCT of Jingxin Zhidong formula (JXZDF) for the treatment of tics in children and adolescents with TS.⁴² Participants were randomized to JXZDF ($n = 60$) or aripiprazole 10 mg ($n = 60$) for 12 weeks. The primary outcome was the reduction in the YGTSS total tic and impairment score. After 12 weeks of treatment, participants receiving JXZDF had significantly lower YGTSS total tic scores than participants receiving aripiprazole, with a mean difference of -2.12 points (95% CI $-3.24, -1.00$). YGTSS impairment scores were not significantly different between groups, with a mean difference of 0.01 (95% CI $-1.5, 1.16$).

There is one Class I RCT of Ningdong granule for the treatment of tics in children and adolescents with TS.⁴³ Participants were randomized to Ningdong granule ($n = 33$) or placebo ($n = 31$) for 8 weeks, with the YGTSS total tic score as the primary outcome. After 8 weeks of treatment, tic severity on the YGTSS was significantly lower in participants randomized to Ningdong granule than those randomized to placebo, with a mean difference of -6.52 (95% CI $-9.80, -3.24$).

Wang studied the use of the ningdong granule as a treatment for tics in a Class II RCT of 120 children and adolescents with TS.⁴⁴ The ningdong granule was compared with placebo, haloperidol, and the combination of the ningdong granule and haloperidol for 8 weeks. The results section did not provide means, SDs, or effect sizes for outcome data, and thus mean differences could not be calculated. The text states that the YGTSS motor, vocal, and total tic scores were significantly reduced ($p < 0.05$) in the ningdong granule, haloperidol, and ningdong granule-plus-haloperidol groups, but not the placebo group.

Additional studies of traditional Chinese medicine for the treatment of tics include one Class IV study of ningdong granule plus haloperidol compared to haloperidol in 90 children and youth with TS⁴⁵; one Class IV study of Qufeng Zhidong recipe compared to haloperidol in 66 children with TS⁴⁶; one Class IV study of Qufeng Zhidong recipe compared to haloperidol in 81 children with tic disorders⁴⁷; and one Class IV study of Tianma Gouteng decoction compared to conventional therapy in 60 children with TS.⁴⁸

Other Integrative and Lifestyle Approaches (See Table S4)

Exercise

There is one Class IV study of the effect of acute aerobic exercise (kickboxing) on tic severity,⁴⁹ and comparing the effect of kickboxing to Tai Chi⁵⁰ on tic severity in 18 youth in an open trial. There is one Class IV study of the effect of six-weeks of aerobic exercise on tic severity in five children with TS and OCD in an open trial.⁵¹

Dance

There is one Class III study comparing the effect of motor activities based on music (the intervention), to motor activities without music (the control), on tic severity in eight adults with

TS.⁵² Participants were randomized to eight 15-min individual sessions with trainers, in which participants performed movements while watching a video, with or without music. The music consisted of two songs, “Gioca Jouer,” and “Testa-Spalla,” which were alternated between sessions. Group level data were incompletely reported in the manuscript. However, the authors report that the song “Testa-Spalla” produced a significantly greater improvement in YGTSS Impairment scores in the music group compared to the control group, $d = 0.81, p = 0.04$.

Music

There is one Class IV study on the effects of music (performance, after performance, mental imagery of performance, and listening to music) on tic severity in an open study of youth and adults with TS,⁵³ and one Class IV study on the addition of music therapy to habit reversal therapy compared to habit reversal therapy alone in a retrospective study of children and youth with chronic tic disorders.⁵⁴

Art Therapy

There is one Class II study of art therapy in 22 children with tic disorders.⁵⁵ Children under the age of 9 were randomly assigned to an art therapy intervention or a waiting list control group. Art activities were implemented in four weekly encounters lasting 45 min. The art activities were delivered by a registered art therapist and consisted of water color painting, clay exercise, coloring mandalas and free drawing. Tic severity was assessed using the YGTSS by an independent rater who was blind to treatment assignment. The authors report a significant group by time interaction on motor and vocal tic severity measured with the YGTSS in the intervention group. The authors hypothesized that the improvement in tics may be due to the beneficial effects of art therapy on psychological stress.

Diet

There is one Class III study of the effects of acute tryptophan depletion in six adults with TS.⁵⁶ In this crossover study, participants were exposed to a diet with or without tryptophan depletion for a two-day period, 1 week apart. There were no effects of condition, time, or a condition by time interaction on clinician ratings of tic severity on the YGTSS.

There is one Class IV study on the efficacy of a gluten-free diet in 29 children and adults with TS.⁵⁷ This was a prospective open-label study with no control condition.

Oral Appliances

There are two Class IV studies of oral appliances versus sham to reduce tic severity in children and adults with TS and chronic tic disorders.^{58,59}

Conclusion

There is limited and low-quality evidence supporting the use of CIM for reducing tics in TS. Most available studies are small and at high risk of bias, limiting the strength of the conclusions that can be drawn. Furthermore, none of the included studies evaluated the effect of CIM on disease specific quality of life. Nonetheless, some approaches show preliminary signs of benefit that may merit further exploration. These interventions may help reduce tic severity and warrant further investigation in larger, well-controlled trials.

We identified four Class I studies that showed positive effects of neurofeedback and traditional Chinese medicine. Sukholdolsky et al⁸ found that real-time fMRI neurofeedback significantly reduced tic severity compared to sham, although the mechanism—improved control of the supplementary motor area—was not supported by secondary outcomes, and the treatment's complexity limits clinical feasibility. Multiple Class I studies of traditional Chinese medicine (5-Ling Granule,³⁹ Ningdong granule,⁴³ Jingxin Zhidong formula⁴²) demonstrated improvements in tic severity superior to placebo or comparable to aripiprazole. However, all studies were conducted in China using proprietary herbal formulas, limiting international applicability due to cultural and regulatory differences. Divergent concepts of disease also may impact interpretation of the approach and proposed mechanism of action. Three Class I studies—on *Lactobacillus plantarum* PS128³⁵ N-acetylcysteine³⁷ and Yi-Gan-san⁴¹ found no benefit over placebo.

The systematic reviews of studies of acupuncture,²⁸ acupuncture and herbal medicine²⁹ and massage therapy³¹ summarized the published Chinese literature on these treatments, with a magnitude of benefit superior to comparators ranging from 2 to 4 points on the YGTSS. As the comparators in these studies consisted predominantly of antipsychotic medications rather than placebo, these findings suggest a major clinical improvement in tics with these treatments. However, trials included in these systematic reviews had high risk of bias, leading to low confidence in the synthesized results.

Despite the possible benefits reported in relation to those complementary and integrative approaches to treatment for which RCT data are available, certain limitations need to be acknowledged. For example, the effectiveness of complementary therapies for TS has been primarily explored in China and Taiwan, with a notable focus on traditional Chinese medicine, acupuncture, and massage. Relying on systematic reviews of the existing literature poses a significant limitation: nearly all the original studies have been published in Chinese, making it difficult to directly assess methodology and results for anyone not fluent in Chinese, which may limit the depth and accuracy of evidence synthesis. Moreover, the availability and accessibility of these treatments outside of these countries remains uncertain and impacts global applicability of these treatments. The proprietary nature of the herbal supplements makes it challenging to replicate results and confounds the picture as it is unclear if it is a single component or a mix of specific components which are contributing to beneficial effects. Understanding the role of these

supplements individually may improve our understanding of their mechanism of action as they may be affecting different neurotransmitters or inflammatory markers through diverse means. The available literature is also limited by the high degree of heterogeneity between interventions within the same class. Such variability limits the conclusions that can be drawn regarding efficacy and underscores the need for standardized and rigorously designed studies across diverse populations and settings.

Given the above-mentioned limitations to the body of evidence, there is currently no robust or compelling evidence that would justify making universal clinical recommendations regarding the use of CIM for people with TS. Clinicians should critically evaluate whether these interventions could be useful in individual people with TS and engage them in shared decision-making. Discussions should include existing evidence, while clearly outlining the limitations and current gaps in our understanding of the role of CIM in people with TS. An integrative approach could be used, considering the cultural background of the patient and selecting the complimentary therapy that is in line with their culture.

We recommend that future research on CIM in TS include trials of acupuncture, massage and traditional Chinese medicine which employ rigorous methodology for allocation concealment and blinded outcome evaluation. Blinding of participants and treating clinicians to treatment allocation can be impossible in some trials of CIM treatments. Even so, risk of bias can be minimized by performing randomized studies with independent blinded outcome assessors. Using patient reported outcomes can also minimize bias, provided patients are not led to believe that randomization to the intervention or control condition may have a superior effect on tics. Studies of acupuncture, massage and traditional Chinese medicine should also be performed outside of China to determine if results can be replicated in other settings. There is a need for high-quality RCTs relating to integrative and lifestyle approaches and the use of supplements. Many CIM modalities have not been assessed for TS, making this an open field for investigators. Future research should also assess any potential effects of CIM on common comorbid conditions with TS, or effect modification related to their presence.

As exercise has been shown to be an effective treatment in other neurodevelopmental and mental health conditions, high quality RCTs of exercise in people with TS are needed. A meta-analysis of RCTs demonstrated that physical exercise can improve attention, executive function and motor skills in children with ADHD.⁶⁰ A systematic review and meta-analysis of physical activity on the mental health of typically developing children and adolescents found that exercise interventions were effective in reducing symptoms of depression and anxiety, improving self-esteem and social competence and reducing stress.⁶¹ Therefore, exercise could have a potential role in TS through management of comorbid symptoms.

In conclusion, evidence to support the use of complementary and integrative medicine for TS is limited in methodological quality and widespread applicability. These limitations prohibit evidence-based recommendations for general use among individuals with TS.

Author Roles

Research project: A. Conception, B. Organization, C. Execution; (2) Statistical Analysis: A. Design, B. Execution, C. Review and Critique; (3) Manuscript Preparation: A. Writing of the first draft, B. Review and Critique.

T.P.: 1ABC, 2ABC, 3A.

C.D.: 1BC, 2B, 3A.

S.A.: 1C, 3B.

P.B.: 1C, 3B.

K.B.: 1C, 3B.

Y.D.: 1C, 3B.

D.G.: 1C, 3B.

A.H.: 1C, 3B.

M.H.: 1C, 3B.

I.M.: 1C, 3B.

D.M.: 1C, 3B.

A.M.E.: 1C, 3B.

P.M.: 1C, 3B.

C.N.: 1C, 3B.

M.S.: 1C, 3B.

J.S.U.: 1C, 3B.

H.S.: 1C, 3B.

K.S.: 1C, 3B.

N.S.: 1C, 3B.

K.T.: 1C, 3B.

D.v.W.: 1C, 3B.

Y.W.: 1C, 3B.

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Data Availability Statement

Data sharing is not applicable to this article as no new data were created or analyzed in this study. ■

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Appendix A

Search Strategies for Medline, PsycInfo, and Cochrane Controlled Register of Trials

Search Strategies

Medline

exp Tics/ or exp Tic Disorders/ or exp Tourette Syndrome/ or "Tourett*" .tw,kf. or (tic adj2 (gestur* or motor* or transient* or vocal* or disorder*)) .tw,kf. or tics.tw,kf

AND

exp Fatty Acids/ or fatty acid*.tw,kf or Omega 6*.tw,kf or exp Plant Oils/ or plant oils/ad or plant oil*.tw,kf or exp Olive Oil/ or olive oil*.tw,kf or exp Complementary Therapies/ or Complementary Therap*.tw,kf or exp Dietary Supplements/sn or dietary supplement*.tw,kf or ((dietary or nutrition* or food* or herbal*) adj2 (supplement or supplements)).tw,kf or exp Beverages/ae or (beverage or beverages).tw,kf. or exp Carbonated Beverages/ or Carbonated Beverage*.tw,kf or exp Coffee/ or coffee*.tw,kf or exp Dietary Sucrose/ or (sugar or sugars or sucrose or "sweetening agent*").tw,kf or exp Diet/ or (diet or diets or dietary).tw,kf or exp Tryptophan/ or tryptophan*.tw,kf or exp Cacao/ae or Cacao*.tw,kf or exp Dietary Carbohydrates/ or carbohydrate*.tw,kf or caffeine*.tw,kf or exp Caffeine/ or exp Magnesium Deficiency/ or (magnesium adj2 deficien*).tw,kf or exp vitamins/ or (vitamin or vitamins).tw,kf or exp Alcoholism/ px or (alcohol* adj3 (overus* or abus* or depend* or addict* or chronic)).tw,kf or Vitamin B 6*.tw,kf or alcoholism*.tw,kf or exp Alcohol Drinking/ or Dietary Fat*.tw,kf or exp Dietary Fats/ad or Dietary Sucrose*.tw,kf or exp diet, Mediterranean/ or mediterranean diet.tw,kf or exp probiotics/ or probiotics.tw,kf

OR

exp exercise/ or Exercis*.tw,kf or exp Physical Fitness/ or fitness*.tw,kf or exp Exercise Movement Techniques/ or exp Reflexotherapy/ or reflexotherap*.tw,kf or exp Physical Therapy Modalities/ or (physiotherap* or "physical therap*").tw,kf or exp Quality of Life/ or Quality of Life.tw,kf or exp Movement/ ph or exp Running/ or Running.tw,kf or exp physical activity/ or Physical activity.tw,kf or Physiological Psychology.tw,kf or exp Sport/ or sport*.tw,kf or exp Exercise therapy/ or exercise therap*.tw,kf or exp Physical exertion/ or Physical exertion.

tw,kf or physical effort*.tw,kf or exp Jogging/ or Jogging.tw,kf or exp recreation therapy/ or recreation therap*.tw,kf

OR

((mind or body) adj2 practic*).tw,kf or exp biofeedback/ or biofeedback.tw,kf or ((breath* or breathing) adj2 therap*).tw,kf or ((breath or breathing) adj2 exercis*).tw,kf or (guided adj2 imag*).tw,kf or exp hypnosis/ or hypnosis.tw,kf or (hypno* adj2 therap*).tw,kf or exp meditation/ or meditation.tw,kf or exp mindfulness/ or mindful*.tw,kf or exp Qigong/ or Qigong.tw,kf or exp Tai Ji/ or Tai Ji.tw,kf Or Tai Chi.tw,kf or exp yoga/ or yoga.tw,kf or exp relaxation therapy/ or (relax* adj2 (therap* or exercise*)).tw,kf or exp music therapy/ or (music adj2 therap*).tw,kf or exp animal assisted therapy/ or ((animal or pet or dog) adj2 therap*).tw,kf or exp occupational therapy/ or (occupational adj2 therap*).tw,kf or exp dance/ or dance.tw,kf

OR

(manipula* adj2 (body or work)).tw,kf or exp acupuncture therapy/ or acupuncture.tw,kf or exp acupressure/ or acupressure.tw,kf or exp manipulation, chiropractic/ or (chiropract* adj2 (therap* or exercis*)).tw,kf or exp physical therapy modalities/ or (physical adj2 (exercise* or therap*)).tw,kf or craniosacral therap*.tw,kf or exp dry needling/ or (dry adj2 needl*).tw,kf or exp massage/ or massage.tw,kf or (massage adj2 therap*).tw,kf or (movement adj2 (therap* or exercise*)).tw,kf or exp manipulation, osteopathic/ or osteopath*.tw,kf or exp musculoskeletal manipulations/ or (musculoskeletal adj2 manipulation).tw,kf or reflexology*.tw,kf

OR

exp complementary therapies/ or (complementary adj2 therap*).tw,kf or (complementary adj2 medicin*).tw,kf or (alternative adj2 therap*).tw,kf or (alternative adj2 medicin*).tw,kf or exp integrative medicine/ or (integrative adj2 therap*).tw,kf or (integrative adj2 medicin*).tw,kf or exp medicine, Ayurvedic/ or Ayurvedic.tw,kf or exp aromatherapy/ or aromatherapy.tw,kf or (aroma adj2 therap*).tw,kf or exp therapeutic touch/ or therapeutic touch.tw,kf or reiki.tw,kf or (heal* adj2 (touch or therap*)).tw,kf or (energy adj2 medicin*).tw,kf or exp holistic health/ or holistic health.tw,kf or functional medicine.tw,kf or exp homeopathy/ or homeopath*.tw,kf or (homeopath* adj2 (medicin* or treatment* or therap*)).tw,kf or exp naturopathy/ or naturopath*.tw,kf or (naturopath* adj2 (medicin* or treatment* or therap*)).tw,kf or exp medicine, Chinese traditional/ or traditional Chinese medicine.tw,kf or exp drugs, Chinese herbal/ or Chinese herbal.tw,kf or exp plants, medicinal/ or exp traditional medicine practitioners/ or traditional medicine.tw,kf or (sleep adj2 therap*).tw,kf or exp hydrotherapy/ or hydrotherap*.tw,kf or exp hyperbaric oxygenation/ or hyperbaric oxygen*.tw,kf or exp oxygen inhalation therapy/ or (oxygen adj2 therap*).tw,kf or normobaric oxygen therap*.tw,kf or proprietary polyherbal.tw,kf or (herbal adj2 medicin*).tw,kf or herbal medicine.tw,kf

OR

(neurostimula* adj2 (wrist band or device*)) or median nerve stimula*.tw,kf or ((dental or ortho*) adj2 device*) or dental splint.tw,kf or splint*.tw,kf or neupulse.tw,kf or exp self-help devices/ or self-help devices.tw,kf

PsycInfo

exp tics/ or exp Tourette Syndrome/ or “Tourett*”).tw. or (tic adj2 (gestur* or motor* or transient* or vocal* or disorder*)).tw. or tics.tw. or tic disorder.tw.

AND

exp Diets/ or diet*.tw. or exp Dietary Supplements/ or dietary supplement*.tw. or exp Fatty Acids/ or fatty acid*.tw. or Dietary Fat*.tw. or exp “Beverages (Nonalcoholic)”/ or exp Tryptophan/ or tryptophan*.tw. or exp Caffeine/ or caffeine.tw. or coffee*.tw. or exp Alcohols/ or exp Alcoholism/ or (alcohol* adj3 (overus* or abus* or depend* or addict* or chronic)).tw. or alcoholism*.tw. or Alcohol Drinking*.tw. or exp Vitamins/ or vitamin*.tw. or Omega-3*.tw. or plant oil*.tw. or olive oil*.tw. or Complementary Therap*.tw. or ((dietary or nutrition* or food* or herbal*) adj2 (supplement or supplements)).tw. or (beverage or beverages).tw. or Carbonated Beverage*.tw. or Dietary Sucrose*.tw. or (sugar or sugars or sucrose or “sweetening agent*”).tw. or (diet or diets or dietary).tw. or Cacao*.tw. or carbohydrate*.tw. or (magnesium adj2 deficien*).tw. or Vitamin B 6*.tw. or Mediterranean diet.tw. or probiotics.tw

OR

exp Exercise/ or Exercis*.tw. or fitness*.tw. or exp Sports/ or sport*.tw. or exp Physical Activity/ or physical activit*.tw. or exp Running/ or Running.tw. or exp “Quality of Life”/ or Quality of Life.tw. or exp Physical Fitness/ or exp Physical Therapy/ or reflexotherapy.tw. or (physiotherap* or “physical therap*”).tw. or Physical activity.tw. or Physiological Psychology.tw. or Physical exertion.tw. or physical effort*.tw. or Jogging.tw.

OR

((mind or body) adj2 practic*).tw. or exp biofeedback/ or biofeedback.tw. or ((breath* or breathing) adj2 therap*).tw. or ((breath* or breathing) adj2 exercis*).tw. or (guided adj2 imag*).tw. or exp hypnosis/ or hypnosis.tw. or (hypno* adj2 therap*).tw. or exp meditation/ or meditation.tw. or exp mindfulness/ or mindful*.tw. or tai ji.tw. or tai chi.tw. or qigong.tw. or exp yoga/ or yoga.tw. or exp relaxation therapy/ or (relax* adj2 (therap* or exercise*)).tw. or exp occupational therapy/ or (occupational adj2 therap*).tw. or exp dance/ or dance.tw. or exp music therapy/ or (music adj2 therap*).tw. or exp animal assisted therapy/ or ((animal or pet or dog) adj2 therap*).tw.

OR

exp acupuncture/ or acupuncture.tw. or acupressure.tw. or exp physical treatment methods/ or exp physical therapy/ or physical therap*.tw. or (chiropract* adj2 (therap* or manipula*)).tw. or (physical adj2 (exercise* or therap*)).tw. or craniosacral therap*.tw. or dry needling.tw. or (dry adj2 needl*).tw. or exp massage/ or massage.tw. or (massage adj2 therap*).tw. or (movement adj2 (therap* or exercise*)).tw. or exp osteopathic medicine/ or osteopath*.tw. or (osteopath* adj2 (therap* or manipula*)).tw. or reflexology*.tw. or (manipulat* adj2 (body or work)).tw

OR

exp aromatherapy/ or aromatherapy*.tw. or (aroma adj2 therap*).tw. or (complementary adj2 (therap* or medicin*)).tw.

or (alternative adj2 (therap* or medicin*)).tw or (integrative adj2 (therap* or medicin*)).tw or ayurveda.tw. or therapeutic touch.tw. or (therap* adj2 (touch or heal* or medicin*)).tw. or healing touch.tw. or reiki.tw. or energy medicine.tw. or integrative medicine.tw. or exp holistic health/ or holistic health.tw. or (holistic adj2 medicin*).tw. or functional medicine.tw. or homeopath*.tw. or (homeopath* adj2 (medicin* or treatment* or therap*)).tw. or naturopath*.tw. or (naturopath* adj2 (medicin* or treatment* or therap*)).tw. or ((traditional or Chinese) adj2 medicine).tw. or exp “medicinal herbs and plants”/ or (sleep adj2 therap*).tw. or exp hydrotherapy/ or hydrotherapy*.tw. or exp oxygenation/ or oxygenation.tw. or ((hyperbaric or normobaric) adj2 oxygen*).tw. or herbal medicine.tw. or (herbal adj2 (medicin* or therap*)).tw.

OR

((neurostimula* adj2 (wrist band or device*)) or median nerve stimula* or ((dental or ortho*) adj2 device*) or dental splint.tw or splint*.tw or neupulse.tw or self-help devics.tw

Central

[mh Tics] or [mh “Tic Disorders”] or [mh “Tourette Syndrome”] or tourette*:ti,ab,kw or (tic NEAR/2 (gestur* or motor* or transient* or vocal* or disorder*)):ti,ab,kw or tics:ti,ab,kw

AND

[mh “Fatty Acids”] or fatty acid*:ti,ab,kw or Omega 6*:ti,ab,kw or [mh “Plant Oils”] or plant oil*:ti,ab,kw or [mh “Olive Oil”] or olive oil*:ti,ab,kw or [mh “Complementary Therapies”] or Complementary Therap*:ti,ab,kw or [mh “Dietary Supplements”] or dietary supplement*:ti,ab,kw or ((dietary or nutrition* or food* or herbal*) NEAR/2 (supplement* or supplements)):ti,ab,kw or [mh Beverages] or (beverage or beverages):ti,ab,kw or [mh “Carbonated Beverages”] or Carbonated Beverage*:ti,ab,kw or [mh Coffee] or coffee*:ti,ab,kw or [mh “Dietary Sucrose”] or (sugar or sugars or sucrose or sweetening NEXT agent*):ti,ab,kw or [mh Diet] or (diet or diets or dietary):ti,ab,kw or [mh Tryptophan] or tryptophan*:ti,ab,kw or [mh Cacao] or Cacao*:ti,ab,kw or [mh “Dietary Carbohydrates”] or carbohydrate*:ti,ab,kw or caffeine*:ti,ab,kw or [mh Caffeine] or [mh “Magnesium Deficiency”] or (magnesium NEAR/2 deficien*):ti,ab,kw or [mh vitamins] or (vitamin or vitamins):ti,ab,kw or [mh Alcoholism] or (alcohol* NEAR/2 (overus* or abus* or depend* or addict* or chronic)):ti,ab,kw or Vitamin B 6*:ti,ab,kw or alcoholism*:ti,ab,kw or [mh “Alcohol Drinking”] or Dietary Fat*:ti,ab,kw or [mh “Dietary Fats”] or Dietary Sucrose*:ti,ab,kw or [mh probiotics] or probiotics:ti,ab,kw or [mh “diet, Mediterranean”] or Mediterranean NEXT diet:ti,ab,kw

OR

[mh exercise] or Exercis*:ti,ab,kw or [mh “Physical Fitness”] or fitness*:ti,ab,kw or [mh “Exercise Movement Techniques”] or [mh Reflexotherapy] or reflexotherap*:ti,ab,kw or [mh “Physical Therapy Modalities”] or (physiotherap* or physical NEXT therap*):ti,ab,kw or [mh “Quality of Life”] or Quality of Life:ti,ab,kw or [mh Movement] or movement:ti,ab,kw or [mh Running] or Running:ti,ab,kw or [mh “physical activity”] or Physical activity:ti,ab,kw or Physiological NEXT Psychology:

ti,ab,kw or [mh Sport] or sport*:ti,ab,kw or [mh “Exercise therapy”] or (exercise NEAR/2 therap*):ti,ab,kw or [mh “Physical exertion”] or Physical NEXT exertion:ti,ab,kw or physical NEXT effort*:ti,ab,kw or [mh Jogging] or Jogging:ti,ab,kw or [mh “recreation therapy”] or (recreations NEAR/2 therap*):ti,ab,kw

OR

((mind or body) NEAR/2 practic*):ti,ab,kw or [mh biofeedback] or biofeedback:ti,ab,kw or ((breath* or breathing) NEXT/2 therap*):ti,ab,kw or ((breath* or breathing) NEAR/2 exercis*):ti,ab,kw or (guided NEAR/2 imag*):ti,ab,kw or [mh hypnosis] or hypnosis:ti,ab,kw or (hypno* NEAR/2 therap*):ti,ab,kw or [mh meditation] or meditation:ti,ab,kw or [mh mindfulness] or mindful*:ti,ab,kw or [mh “Qigong”] or Qigong:ti,ab,kw or [mh “Tai Ji”] or Tai NEXT Ji:ti,ab,kw or [mh yoga] or yoga:ti,ab,kw or [mh “relaxation therapy”] or (relax* NEXT/2(therap* or exercise*)):ti,ab,kw or [mh “music therapy”] or (music NEAR/2 therap*):ti,ab,kw or [mh “animal assisted therapy”] or ((animal or pet or dog) NEAR/2 therap*):ti,ab,kw or [mh “occupational therapy”] or (occupational NEAR/2 therap*):ti,ab,kw or [mh dance] or dance:ti,ab,kw

OR

(manipula* NEAR/2 (body or work)):ti,ab,kw or [mh “acupuncture therapy”] or acupuncture:ti,ab,kw or [mh acupressure] or acupressure:ti,ab,kw or [mh “manipulation, chiropractic”] or (chiropract* NEAR/2 (therap* or exercis*)):ti,ab,kw or [mh “physical therapy modalities”] or (physical NEAR/2 (exercise* or therap*)):ti,ab,kw or craniosacral therap*:ti,ab,kw or [mh “dry needling”] or (dry NEAR/2 needl*):ti,ab,kw or [mh massage] or massage:ti,ab,kw or (massage NEAR/2 therap*):ti,ab,kw or (movement NEAR/2 (therap* or exercise*)):ti,ab,kw or [mh “manipulation, osteopathic”] or osteopath*:ti,ab,kw or [mh “musculoskeletal manipulations”] or reflexology*:ti,ab,kw

OR

[mh “complementary therapies”] or (complementary NEAR/2 therap* or medicin*):ti,ab,kw or [mh “medicine, Ayurvedic”] or Ayurvedic:ti,ab,kw or [mh aromatherapy] or aromatherap*:ti,ab,kw or (aroma NEAR/2 therap*):ti,ab,kw or [mh “therapeutic touch”] or therapeutic NEXT touch:ti,ab,kw or reiki:ti,ab,kw or (heal* NEAR/2 (touch or therap*)):ti,ab,kw or (energy NEAR/2 medicin*):ti,ab,kw or [mh “integrative medicine”] or integrative NEXT medicine:ti,ab,kw or [mh “holistic health”] or holistic NEXT health:ti,ab,kw or functional medicine:ti,ab,kw or [mh homeopathy] or homeopath*:ti,ab,kw or (homeopath* NEAR/2 (medicin* or treatment* or therap*)):ti,ab,kw or [mh naturopathy] or naturopath*:ti,ab,kw or (naturopath* NEAR/2 (medicin* or treatment* or therap*)):ti,ab,kw or [mh “medicine, Chinese traditional”] or traditional NEXT Chinese:ti,ab,kw or [mh “drugs, Chinese herbal”] or Chinese NEXT herbal:ti,ab,kw or [mh “plants, medicinal”] or [mh “traditional medicine practitioners”] or (sleep NEAR/2 therap*):ti,ab,kw or [mh hydrotherapy] or hydrotherap*:ti,ab,kw or [mh “hyperbaric oxygenation”] or hyperbaric NEXT oxygen*:ti,ab,kw or [mh “oxygen inhalation therapy”] or oxygen NEXT therap*:ti,ab,kw or normobaric oxygen therap*:

ti,ab,kw or proprietary polyherbal:ti,ab,kw or (herbal NEAR/2 medicin*):ti,ab,kw

OR

(neurostimula* NEAR/2 (wrist band or device*)):ti,ab,kw or median nerve stimula*:ti,ab,kw or ((dental or ortho*) NEAR/2 device*):ti,ab,kw or neopulse:ti,ab,kw or dental splint:ti,ab,kw or splint*:ti,ab,kw or [mh "self-help devices"] or (self-help NEAR/2 device*):ti,ab,kw

Supporting Information

Supporting information may be found in the online version of this article.

Table S1. Mind Body Practices

Table S2. Supplements

Table S3. Traditional Chinese Medicine

Table S4. Other Integrative and Lifestyle Approaches