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Acupuncture for the Treatment of Diabetes Related Distal Sensory Neuropathy: A Review of Study Designs and Quality of Randomized Controlled Trials

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ABSTRACT

Diabetes affects nearly every organ system in the body, including the peripheral nervous system, and leads to the development of distal sensory peripheral neuropathy (DSP) in roughly 50% of patients. Between 30% to 50% of patients with DSP experience pain and impaired quality of life. Dissatisfaction with currently available pharmacological treatments for neuropathic pain is common, primarily due to limited effectiveness and potential for adverse side effects. Acupuncture, a non-pharmacologic intervention, is often used in the management of chronic pain and is widely available and acceptable to many patients. In this narrative review, we describe clinical research related to acupuncture and diabetes related DSP management including meta-analyses, systematic reviews, and randomized controlled clinical trials (RCTs). Data from the few clinical trials available support the use of acupuncture to reduce neuropathic pain including DSP pain; however, available studies suffer from methodological weaknesses including inadequate blinding, sample size justification, lack of well-designed controls, and gaps in reporting. These limitations highlight a critical gap and an unmet need for more rigorous and robust clinical research requiring the use of Standards for Reporting Clinical Trials of Acupuncture (STRICTA) guidelines as a design, implementation, and reporting template.

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Introduction

More than 400 million adults have diabetes mellitus (DM), including an estimated 38 million in the United States (US), where the associated economic burden exceeds 400 billion dollars annually [1-3]. Diabetes affects nearly every organ system in the body, including the peripheral nervous system, and leads to the development of distal sensory peripheral neuropathy (DSP) in roughly 50% of patients [1,4]. With the progressive deterioration of peripheral nerve function, DSP patients may experience a range of intermittent or persistent neuropathic symptoms in their extremities-including allodynia, paresthesia, burning pain, muscle weakness, and others-that interfere with sleep, healthy mood, balance, and life quality and increase the risk for falls, foot ulcers and amputations, disability, and death [1,4]. Diabetes-related neuropathies cost US patients and payers 10 billion dollars annually [1].

About 30% to 50% of peripheral neuropathy patients experience pain and consequent reductions in quality of life [1]. Patients report low rates of satisfaction with currently available pharmaceutical treatments for neuropathic pain, including tricyclic antidepressants, serotonin-norepinephrine reuptake inhibitors, gabapentinoids, and sodium channel blockers, which are often ineffective in controlling their pain [5-6]. These agents are also commonly associated with side effects-including dry mouth, urinary retention, orthostatic hypotension, and nausea-further limiting their use [6]. Opioid analgesics, while effective in the short-term, are increasingly considered a non-option for long-term use due to well-documented risks for dependency and overdose [6]. Given the high prevalence, disease burden, progressive natural history of DSP and the limited efficacy of conventional oral analgesics, there is a pressing need

for effective non-pharmaceutical therapies (NPTs) for treating neuropathic pain. For over 3000 years, acupuncture has been used to prevent and treat diseases in the East. It has become widely accepted and available in the West for managing a growing list of indications, including neuropathic pain [7-8].

Acupuncture research requires addressing unique challenges, including selecting points and adapting Traditional Chinese Medicine (TCM) to comport with Western disease definitions and protocols. The design and adminstration of a placebo (sham) control for effective blinding; and the need to account for, control for, and report on administration aspects (e.g., needling style, technique, depth, retention duration) is necessary so that accuracy and uniformity is possible and studies can be replicated [9-10]. A lack of consensus around how to best manage these challenges has contributed to considerable inconsistencies in trial design and execution and low overall evidence quality [9-10].

Efforts to elevate quality and reporting in acupuncture clinical trials in 2001 led to the creation of the Standards for Reporting Interventions in Clinical Trials of Acupuncture (STRICTA) guidelines, based on previously published CONSORT guidelines for clinical trial reporting more generally [11]. With its more recent update in 2010, STRICTA adherence involves reporting on six items and 17 subitems related to acupuncture rationale, details of needling, treatment regimen, other components of treatment, practitioner credentials and experience, and details regarding control or comparator intervention [11]. While the establishment of STRICTA was an important milestone on the road to more scientific rigor in the evaluation of acupuncture, its value has, to date, been limited by inconsistent adherence.

Purpose and Methods

In this narrative review, we describe the clinical research-including meta-analyses, systematic reviews, and randomized controlled clinical trials (RCT) - assessing the efficacy of acupuncture for the treatment of diabetes-related DSP. Our objectives are threefold: to identify available RCTs reporting on the use of manual acupuncture for the treatment of diabetes-related DSP, characterize acupuncture efficacy according to the current knowledge base, and assess opportunities for quality improvement in future research.

We used a two-stage process to evaluate the current state of clinical research in relation to the use of manual acupuncture for the treatment of diabetes-related DSP. First, we searched the PubMed publication database for relevant meta-analyses and reviews, published through November 2023 in English in full text, that included at least one trial meeting these criteria: prospective RCT that evaluated administration of manual acupuncture without adjunctive treatment (other than glucose-lowering or usual care) for the treatment of diabetes-related DSP. For reviews with a broader scope (e.g., treatment of peripheral neuropathic pain), we focused exclusively on diabetes-related DSP trials. For DSP reviews that included Chinese-language only or both Chinese- and English-language reports, we reviewed authors' analysis, commentary, and conclusions, then searched for clinical trial reports to verify, where possible. We then searched for and reviewed English language publications of individual prospective RCTs in which manual acupuncture was compared with usual care, waitlist control, another intervention, or placebo (sham) acupuncture in treating diabetes-related DSP. Studies that evaluated electroacupuncture, laser acupuncture, warm needling, or other acupuncture variations were excluded if they did not include a manual acupuncture-only arm.

We looked at studies which included in one or more meta-analyses or systematic reviews. Then, we searched for studies that might have been omitted or published after the most recent review.

Findings

We found ten reviews of acupuncture for diabetes-related DSP clinical trials that met the above criteria, including three meta-analyses, one overview of systematic reviews, five systematic reviews, and one narrative review [12-21]. Separately, we identified six publications of RCTs of manual acupuncture vs. usual care (1), waitlist control (1), another intervention (2), or placebo (sham) acupuncture (2) for the treatment of diabetes-related DSP, five of which were cited in one or more of the reviews and one of which was recently published and has not been mentioned in a review to our knowledge [22-27].

Meta-Analyses

Three meta-analyses were identified. Li and colleagues conducted a meta-analysis and systematic review of RCTs in the English or Chinese language literature through April 2023 that investigated manual acupuncture as mono- or adjunctive therapy for treating neuropathic pain secondary to type I or II diabetes [12]. Nineteen trials were identified and included in the meta-analysis: 17 from China, one from the United Kingdom (UK), and one from the US. The median sample size was 64 subjects (range 34- 96). Treatments, methods, and outcome measures of included trials differed. Fifteen studies compared acupuncture plus basic treatments, medications, or both to the same intervention(s) without acupuncture. Two studies compared acupuncture with a non-acupuncture intervention, such as medication or acupoint tapping [28, 29]. One trial by Cheng et al. reportedly compared true acupuncture with superficial acupuncture at non-points, indicating the potential for a well-blinded study [30]. However, according to Li and colleagues, the study had a high risk of performance bias due to insufficient provider and/or participant blinding [12]. Only one trial compared acupuncture to placebo (sham) control and achieved and verified participant blinding [22]. The meta-analysis showed that manual acupuncture improved pain and clinical neuropathy and partially improved quality of life in patients with DM. However, the authors concluded that a lack of clarity regarding randomization procedure, allocation concealment, and blinding in studies performed to date introduced a significant risk for selection and performance biases and underscored the need for further larger-scale, high-quality RCTs. They suggested future studies aim to determine acupuncture type, protocol, point selection, needle depth, frequency, and cumulative dose [12].

In a separate meta-analysis and systematic review, Dimitrova and colleagues in the US analyzed RCTs published in English through 2015 in which acupuncture was compared to conventional medical or sham therapy for the treatment of peripheral neuropathy due to a range of etiologies, including four trials among patients with DM [13]. Authors reported that due to the poor study quality of most published trials, only four diabetes-related DSP studies met their criteria for inclusion: three that compared manual acupuncture vs oral or intravenous medication [27,31-32] and one that compared electroacupuncture to a regimen of oral and intramuscular B-vitamins [33]. Meta-analysis of the diabetes-related DSP study subset revealed significant improvements in subjective (neurologic symptoms, composite scores) and objective (neurologic examination, nerve conduction velocity) outcomes attributable to acupuncture [13,27,31-32]. They further suggested that acupuncture might be more effective than medical treatments, including intravenous vitamin B12, oral mecobalamin, and oral inositol [27,31-32].

The authors noted significant study deficits and described five categories of potential bias from methodological problems among included studies [13]. First, there was a lack of methodological standardization in the included studies and in acupuncture research in general. Treatment specifications included acupoint selection and sequence, number and types of needles, needle manipulation, acupuncture modality, and total acupuncture dose [13]. For example, in the RCT by Zhang and colleagues, point selection varied somewhat according to individual presentation [27]. In addition to standardization, authors underscored the importance of investigating manual acupuncture in its pure form (without adjunctive medications, herbs, etc.) [13]. Second, most studies-including those for diabetes-related DSP-failed to include sample size calculations and may have been underpowered. Third, there were methodological problems with control and blinding. Within this meta-analysis none of the diabetes-related DSP studies used a placebo (sham) control; all lacked participant, practitioner, and outcome assessment blinding. Fourth, there was potential bias related to a higher number of visits in the acupuncture-treated cohorts compared to untreated cohorts in some studies. This factor might inflate outcome expectancy in the former group. Fifth, outcome measures used in the studies were varied (e.g., global scales vs. sensation-specific measures) [13]. Only one diabetes-related DSP study in this series assessed nerve conduction, an objective measure of treatment effect [32].

A third meta-analysis was performed by Xioing and colleagues in Beijing, China [14]. They analyzed 40 RCTs in which acupuncture was used to treat diabetes-related DSP. They compared the efficacy of four modalities: manual acupuncture, electroacupuncture, needle-tapping acupuncture, and methods involving warm-needling and herbal applications [14]. All included studies were conducted in China; none were placebo (sham)-controlled. The authors note poor methodologic rigor of most of the included studies and recommended that their results be interpreted cautiously [14].

Overview of Systematic Reviews

Yu and colleagues presented an overview of systematic reviews of RCTs that evaluated acupuncture for the treatment of diabetic peripheral neuropathy [15]. Eighteen papers met the inclusion criteria-2 qualitative and 16 quantitative reviews-and were evaluated for quality of methodology and reporting. Authors noted that evidence supports acupuncture efficacy in reducing symptoms and improving nerve conduction velocity in patients with diabetes-related DSP; however, significant deficits were noted, and overall methodological quality was considered "extremely low" [15]. Of eighteen included systematic reviews, four were available in English as full text, enabling further review by our team [13,16,19,34]. One focused exclusively on acupoint injection and was therefore omitted from our review [34]. One was available in English as an abstract only [17].

Other Systematic Reviews

In addition to the review by Yu et al., five other systematic reviews were identified. Nash and colleagues in Sydney, Australia, reviewed clinical trials through June 2017 in which acupuncture was used in the treatment of lower limb diabetes-related peripheral neuropathy, reporting on before and after outcomes [16]. Ten studies conducted in China (4), the UK (2), the US (2), Korea (1), and Ireland (1) were included. The intended meta-analysis was not possible due to the limited number of high-quality studies and heterogeneity among those included, e.g., acupoints, number of treatments, needle retention time, etc. However, researchers offered a detailed appraisal of study quality including the use of the Cochrane risk of bias tool and STRICTA guidelines.

Only two studies in the Nash et al. series were RCTs that compared acupuncture with a placebo (sham), one by Tong et al. 2010 and a pilot RCT by Garrow et al. 2014, discussed below [22-23]. The authors concluded that more high-quality research using robust comparators, specifically sham acupuncture, is needed. They urged that future studies embrace current standards for reporting and acupuncture delivery quality as outlined in STRICTA [16].

In a second systematic review (available as an abstract only), Amato Nesbit and colleagues, Maryland, U.S., performed a systematic review of 23 RCTs of non-pharmacologic treatments for diabetes-related DSP [17]. As the review included only one study of acupuncture, no conclusions could be drawn [17,35].

Thirdly, a Cochrane systematic review of manual acupuncture RCTs for the treatment of chronic neuropathic pain was published in 2017 by Ju and colleagues in Shanghai, China, and Nottingham, UK [18]. Their search yielded only six studies that met minimal inclusion criteria (e.g., randomized, manual acupuncture only, active or placebo (sham) comparator, eight weeks or longer treatment duration). Three studies assessed acupuncture for the treatment of diabetes-related DSP specifically vs. placebo (sham) control, mecobalamin combined with nimodipine, or inositol [22, 36, 27]. Authors found a significant risk for bias among all studies related to the blinding procedure, sequence generation, allocation concealment, selective reporting, and other deficits. They stated that due to a paucity of reliable data, conclusions could not be drawn regarding the use of acupuncture for diabetes-related DSP treatment, and larger, placebo-controlled RCTs are needed [18].

Fourthly, Chen and colleagues performed a systematic review of RCTs through 2013 of manual acupuncture for the treatment of diabetes-related DSP [19]. Despite searching multi-lingual medical literature, only trials conducted in China were included [19,34]. Twenty-five studies were reviewed, although inclusion criteria were not clearly stated [13]. None of the included reports satisfied CONSORT and STRICTA guidelines, and conclusions could not be drawn due to methodological flaws among the studies [13,19].

Lastly, in a separate review by Bo and colleagues in Tianjin and Ganzu Province, China, researchers appraised the quality of RCTs through 2011 evaluating acupuncture for treating diabetes-related DSP against STRICTA and CONSORT reporting guidelines [20]. Of the 75 reviewed, no study fulfilled all reporting requirements. The authors judged study quality as moderate-to-low overall. Thus, an intended systematic review was not conducted [13,20]. Authors urged acupuncture researchers to implement more rigorous study designs and follow STRICTA reporting guidelines so that future meta-analyses might be possible [20].

Narrative Review

We identified one narrative style review. Cho and colleagues published a narrative review of in vivo research on the use of acupuncture for the treatment of diabetes-related DSP that included five animal studies and ten human clinical trials [21]. The authors maintained that, despite heterogeneity among methods, techniques, and outcome assessments, the results of included clinical trials were positive and supported the use of acupuncture for treating diabetic neuropathy. Their analysis revealed a preliminary benefit for manual acupuncture compared with laser acupuncture. They also analyzed the array of acupoints studied to date and offered

insights into acupuncture's potential analgesic mechanisms of action [21].

RCTs of Manual Acupuncture vs Comparator

As mentioned, we searched for publications of RCTs in which manual acupuncture was compared with relevant comparators (e.g., usual care, waitlist control, another intervention, or placebo (sham) acupuncture) in treating diabetes-related DSP. We found six such trials available in English in full-text: 5 that appeared in one or more of the reviews cited above and one published recently and thus not referenced in the above reviews [22-27].

Acupuncture vs Placebo (sham) Control

We identified two studies that evaluated manual acupuncture for diabetes-related DSP treatment against a placebo (sham) control arm [22-23]. One was a single-blind, placebo-controlled pilot RCT by Garrow and colleagues at clinics in Manchester, UK, that compared ten weeks of once-weekly lower limb acupuncture vs non-penetrating placebo (sham) control in participants with painful diabetic neuropathy [22]. Fifty-nine individuals were enrolled, and 45 completed treatment. True and sham acupuncture were delivered at the same acupoint series on the lower limbs. Sham treatment was administered using the Park sham acupuncture device (AcuPrime; Exeter, UK); results showed that, compared to sham, acupuncture was associated with improvement in pain, neuropathy symptoms, and sleep across multiple metrics [21-22].

Despite the use of placebo-controlled study design, several factors limit the interpretation of the trial [12,16,18]. They noted a 24% drop-out rate, which may have contributed to type II errors [22]. More than twice as many participants dropped out from the sham treatment arm compared to the true treatment arm (10 vs 4), the significance of which needed to be clarified [22]. Secondly, evidence quality was considered "very low" by other reviewers as there was potential for bias related to attrition rates, outcomes selection, blinding methods, outcomes assessment blinding, and incomplete or imprecise data presentation [12,16,18]. Additionally, in meta-analyses, studies that use the Park or similar sham acupuncture devices are associated with low credibility of blinding, even when author-reported blinding credibility was satisfactory [37-38]. Nonpenetrating-style sham devices, including the Park, involve a tube stabilized by a ring at the point of skin contact and require the application of adhesive tape to stay in place. The mechanism affects the technique of placement, limits body sites where needles may be placed (e.g., feet and toes), and can cause pain on removal and a distraction, all of which may affect the integrity of the study [39]. Also, some sham acupuncture devices produce an audible click, which could also interfere with blinding. While the authors of the above study concluded that blinding was maintained, their assessment was based on a post-hoc analysis of interviews conducted three months following the final visit [22].

Another concern with their placebo (sham) control was that they used true acupoints, which may elicit a therapeutic effect (i.e., not be fully inert) and interfere with the detection of an isolated verum acupuncture treatment effect [22,37,39-41]. Unless placebos (shams) are carefully designed and void of secondary cues, authors indicate that sham devices can produce an effect sometimes stronger than pharmaceutical placebos [40,42,43]. Delivery of placebo (sham) acupuncture to non-points would reduce risk for inadvertent stimulation of points and better serve an acupuncture RCT protocol. Lastly, although this feasibility study was considered successful, we did not identify a larger follow-up study that verified the results.

In a separate placebo-controlled pilot RCT by Tong and colleagues in Changchun, China, patients with diabetes-related DSP (N=42) were randomized to receive either verum acupuncture or placebo (sham) acupuncture once daily for 15 sessions [16,21,23]. The method of verum acupuncture was inserting needles (0.3mm diameter 50mm length) at five acupoints at 1.2-2.3cm depth, needle manipulation to elicit De qi response, and needle retention for 30 minutes. The sham approach involved the use of the same size and style of needles at the same acupoints and retention but inserted to only 0.3 cm depth without inducing De qi. Researchers found that acupuncture treatment reduced the extent and severity of pain, numbness, and altered temperature perception in the lower extremities and the severity and extent of rigidity in the upper extremities compared to sham treatment. Further measures of motor and sensory nerve function improved with acupuncture, but not sham [23].

There are several notable limits to the interpretation of this study. First, acupuncture was administered daily for 15 days. While common in the East, daily acupuncture may be less acceptable to patients in the West; reproducing a study using a daily acupuncture regimen could be challenging. Second, although comparison vs placebo (sham) control was done, the sham style may not have been optimal. This trial was excluded from the meta-analysis by Dimitrova et al. based on "improper control condition" [13]. Further, there was a lack of clarity regarding allocation concealment and possibly selective reporting [16]. In addition, the study had significant limitations, including a lack of presentation of differential diagnosis, a lack of medical literature support for acupoint selection, and a failure to describe practitioner training and credentialing [16].

Acupuncture vs Waitlisted Control

An RCT study by Dietzel et al. on sixty-two participants with diabetes-related neuropathy compared acupuncture vs. a waitlist control group that received usual care [24]. The primary outcome was overall complaints on the visual analog scale (VAS); secondary outcomes included assessments of pain, emotional aspects of pain, and quality of life showed improvement on both measures [24]. However, the study had a few important limitations. The trial was unblinded as it was not placebo (sham)-controlled, leaving open a risk that knowledge of receiving treatment might have influenced participants' impression of the effect. Another issue, aside from a small sample size, was that the acupuncture intervention was only semi-standardized, as the needling of 9 additional points was permitted and variably performed. There was also mention that heat was applied but the method of application and timing was not specified. Also of note, study groups had imbalances of pain scores at baseline, the impact of which are unclear: proportion with neuropathy symptoms > 5 years (higher in control group) and expectation for improvement with acupuncture treatment (higher in intervention group) [24].

Manual Acupuncture vs Laser Acupuncture vs Sham Laser Control

Myer-Hamme and colleagues conducted a 3-arm, partially double-blinded RCT acupuncture and laser acupuncture for treating diabetic neuropathy that compared manual acupuncture, laser acupuncture, and a placebo (sham) laser acupuncture procedure [25]. The manual acupuncture part of the study was considered "single-blinded" and was not sham-controlled; the laser acupuncture part was "double-blinded" and used a placebo-laser that mimicked the verum laser procedurally but did not emit light. Participants received ten sessions over ten weeks. Nerve

conduction studies of sensory and motor nerves and patient-reported outcome measures were assessed [21,25].

One hundred eighty participants with type II diabetes and DSP were enrolled; 172 completed the trial. Results showed improved sensory nerve conduction velocity (SNCV) among active treatment groups compared with laser placebo and improved motor nerve conduction velocity (MNCV) with manual acupuncture. All 12 queried items on patient-reported outcomes improved in the manual acupuncture group, compared to 11 and 9 items in the laser-treated and laser placebo-treated groups, respectively. Although the study was well powered, several factors undercut its scientific rigor and limit the interpretation of results. The methods for administering laser acupuncture and placebo (sham) laser were not fully described. Additionally, researchers opted not to include a control for the manual acupuncture group, e.g., a placebo (sham) intervention that mimicked manual acupuncture or, barring that, a waitlisted or usual care control group. As constructed, participants randomized to manual acupuncture were likely aware of their study group assignment, which may have impacted patient-rated outcomes.

Acupuncture vs Usual Care

A single-center pilot, RCT by Chao and colleagues, compared 12 weeks of once- or twice-weekly lower limb acupuncture delivered in a group setting vs. usual care among patients with type II diabetes and painful diabetic neuropathy [26]. Results showed pain reduction at 6 and 12 weeks among acupuncture-treated patients compared to the control group. However, other endpoints were unmet, including pain reduction vs. control at the 18-week follow-up, improved quality of life, physical functioning, and neuropathic symptoms. Limitations of the study included low sample size due to recruitment challenges, lack of a proper placebo (sham) comparator, and lack of blinding [12,26].

Acupuncture vs Oral Agent

In an RCT by Zhang and colleagues in China (N=65), five 2-week courses of daily acupuncture (separated by 4-day pauses; 70 total sessions) were compared with a control group treated with three times daily oral inositol (2 g per day) in patients with diabetes-related DSP [27]. At the end of the study, efficacy rates (defined as "marked relief" or "improvement" on physical neurologic exam and self-report of symptoms) for acupuncture and inositol were 88% and 64%, respectively ($P<0.05$).

This study has been criticized in several reviews above, has been criticized for lack of placebo (sham) control arm, lack of blinding, omission of sample size calculation and statistical plan in methods, imbalance in medical attention provided to the two groups, and absence of a validated tool for outcome assessment [13]. Ju et al., in their Cochrane review, cited other significant gaps in Zhang et al.'s reporting, including a description of the randomization sequence procedure, allocation concealment, and outcome data [18]. In their review, Nash and colleagues Zhang's study cited acupuncture administration quality issues related to differential diagnosis, needle description, rationale for acupoint selection, and practitioner training and registration [16].

Discussion

Diabetes-related distal sensory peripheral neuropathy is a chronic, debilitating, often painful condition affecting the quality of life in 50% of individuals affected by DM. Medications prescribed to manage diabetes-related DSP pain (e.g., non-narcotic and narcotic analgesics, opioids, anti-depressants, anticonvulsants, and topical agents) may be poorly tolerated and are largely ineffective. Acupuncture is a non-pharmacologic intervention that is often recommended and well-received by patients.

Overall, the literature assessing acupuncture for diabetes-related peripheral neuropathic pain is limited by design flaws and a lack of scientific rigor, which limits the interpretation and generalizability of estimating the efficacy of acupuncture for this condition. This is underscored by the fact that, among research teams that set out to review and analyze studies on acupuncture for diabetes-related DSP, at least five teams were unable to fulfill their initial objectives and/or reported inconclusive results due to a lack of standardized trial design, incomplete reporting, and/or insufficient availability of high-quality data. [16-20].

Absent from the literature are randomized, well-blinded, placebo (sham)--controlled trials evaluating manual acupuncture for diabetes-related DSP. RCTs addressing non-pharmacological interventions require well-planned placebo/sham comparators to ensure relative safety and efficacy [44]. We identified only two individually reported clinical trials and a reference to a third that compared manual acupuncture to some form of sham acupuncture and reported their methodology at least partially. Sham designs varied, and their effectiveness is unclear [12,22,23,30]. In neither study were participants asked to wear a blindfold to reduce visual cues, and both studies opted to deliver placebo (sham) acupuncture to true acupoints, potentially introducing placebo-induced effects. One used a retractable sham acupuncture delivery device that has been associated with limitations [37]. Beyond those related to placebo (sham) design and blinding, other serious design and performance deficiencies were widespread, including, most commonly, questionable outcomes assessment selection, issues with recruitment and retention, and failure to control for varied levels in medical attention [13,22,24,26,27].

Further, most studies within the current body of acupuncture for diabetes-related DSP literature did not comply with STRICTA reporting. Gaps in reporting are problematic because they allow for vagueness where there should be precision and transparency; they also make it difficult to appraise methodology, understand and compare results, and replicate the study. Clear, complete reporting is critical in the growing field of acupuncture. Western readers expect compliance with scientific standards and are likely to be unfamiliar with the nuances of Eastern medical techniques. Among the papers reviewed, we found reporting gaps and nonadherence to STRICTA guidelines to be widespread, including most commonly reporting of sample size calculations, scientific support/rationale for point selection, differential diagnosis, procedures for randomization and allocation concealment, practitioner training and credentials, and outcomes reporting [12,13,16,18,22,23,27]. A limitation of the current review is that we did not access non-English language publications. However, as mentioned, our search produced several English-language summaries of non-overlapping acupuncture trials performed and published in China, which have been included in this report.

Acupuncture has been shown, at least preliminarily, to improve pain, neuropathic symptoms, sleep , physical examination findings, nerve function studies and quality of life, among DSP patients is certainly encouraging. Combined with its reputation as a well-accepted and well-tolerated procedure and an expanding list of accepted indications, further study of acupuncture for diabetes-related DSP is warranted and should be fast-tracked given the enormous prevalence of diabetes and the urgent need for more effective DSP treatments [12-15,22-27].

Future studies should address limitations reported in the literature to better characterize and quantify acupuncture efficacy by comparing acupuncture to well-designed placebo (sham) controls, embracing all aspects of the scientific method, and complying with or exceeding CONSORT and STRICTA guidelines for design and reporting. Trial protocols should be designed to minimize differences in participant exposure to secondary cues, as study settings and placebo intervention designs have been shown to influence outcomes in clinical trials investigating pain [45]. Further, greater detail in descriptions of the study protocol (session number and frequency, session duration, intersession interval, timing of outcome data collection, blinding), treatment protocol (rationale of point selection, point placement, control conditions, acupuncturist licensure, and training), and research setting (subject preparation, treatment room milieu, staff/subject interactions) are needed.

In summary, a review of meta-analyses, reviews, and clinical trials revealed preliminary albeit low-quality evidence supporting the use of acupuncture for the treatment of diabetes-related neuropathic pain. There is an unmet need for more robust clinical research using STRICTA guidelines as a design, implementation, and reporting standard. Further, acupuncture researchers should strive to meet or exceed standards used in pharmaceutical clinical trials, including greater use of blinded, placebo (sham)-controlled RCT study design. The current lack of reliable evidence for treating diabetes-related DSP with acupuncture has important public health implications as it restricts accessibility to patients who may benefit.

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