



Contents lists available at ScienceDirect

Integrative Medicine Research

journal homepage: www.imr-journal.com

Editorial

Is acupuncture dose dependent? Ramifications of acupuncture treatment dose within clinical practice and trials



Acupuncture is known to have been practiced for more than 2000 years in China and then throughout East Asia. However, it only began to be studied in controlled clinical trials starting in the second half of the 20th century and in the West starting in the 1970s. Over that period of time, a pattern has emerged with trials carried out in countries such as China, Korea, and Japan tending to identify acupuncture as having a consistently high rate of effectiveness, often in the 90% range. Conversely, trials in Western countries tend to show lower overall effectiveness rates and to demonstrate a great deal of variation in effectiveness rates between different trials.¹ Some have gone so far as to say that the consistently high effectiveness rates of Chinese trials indicate those trials cannot be trusted.² Others have countered that many Western trials showing relatively lower effectiveness rates were conducted using poor clinical protocols and were carried out by acupuncturists with limited training.²

Since acupuncture began to be studied in controlled trials, much has been written about the challenges associated with acupuncture research that fall into two primary categories: issues with the quality of trial design/implementation and issues with the quality of the clinical protocols.^{1,3-7} Examples of trial design/implementation issues include factors such as adequate sample sizes, blinding, allocation concealment, randomization, dropout rates, etc. These issues are essentially the same for any clinical trial.⁸ Examples of clinical protocol issues include such things as the training/skill level of the acupuncturists, the frequency and total number of treatments administered over a specific time frame, the ability to properly select and locate the acu-points, various aspects of needling skills, and whether or not needle sensations such as de qi are obtained.⁹ While concerns over the training/skill level of the acupuncturists and frequency/total number of treatments are similar to those for trials done on a variety of therapies, the point selection/location and needling skills are unique to the study and practice of acupuncture.

Studies utilizing suboptimal protocols in trial design/implementation can lead to false positives while studies utilizing suboptimal protocols in aspects of clinical quality can lead to false negatives. Out of these two categories, more attention has been paid to aspects of trial design/implementation within acupuncture trials and less to issues of clinical quality protocols. This is understandable, considering that trial

design/implementation protocols are well established and relatively easy to assess while clinical quality issues regarding acupuncture are largely not established and thus not easy to assess.

To date, there are no published, industry-vetted clinical practice guidelines for the application of acupuncture for any of the many conditions for which it is utilized and studied. In the absence of such clinical practice guidelines, researchers (and many practicing acupuncturists) with varying degrees of acupuncture training are left to their own devices in trying to assess the clinical aspects of point selection/needling techniques and frequency/total number of treatments over time. This has led to a great variation in the clinical protocols utilized in different trials.

While the issue of clinical quality in acupuncture trials was identified as a cause for concern quite early on and a few studies have tried to address those issues, practical solutions for how to make progress in the area of clinical quality guidelines in acupuncture research have been slow to emerge.¹¹ This article addresses issues relating to clinical quality in acupuncture trials and offers suggestions for improving the quality of acupuncture research.

Utilization Management policy and adequate dose vs optimal dose (maximum therapeutic benefit)

In order to highlight clinical quality issues in acupuncture research it is helpful to consider how U.S. medical insurance policy providers develop and administer what is referred to as “Utilization Management” (UM) policies also sometimes referred to as “medical necessity” policies.

While there are variations in exactly what any medical insurance policy is legally obligated to cover (pay for), a general rule is that they are required to cover medical care that can be expected to cause a health benefit for a policyholder and are not required to cover care unlikely to improve a policyholder's health. When a therapy reaches a point where no further benefit can reasonably be expected, this is known in medical legal terms as reaching maximum therapeutic benefit (MTB). A guiding and often legally binding principle in the development of UM policies is that they need to provide coverage until MTB is reached but not past the point of MTB being reached.

In essence, UM policies attempt to manage what both patients and healthcare providers would have as their goal in clinical care; continue therapy as long as it is improving the patient's health and discontinue therapy when it is found to not improve or no longer improve the patient's health. In order to accomplish this, UM policy development will typically involve an extensive review of published research and clinical guidelines as well as a consensus building process with clinical experts. Of particular importance is to establish both how much of a particular therapy is needed to allow for measurable improvement to first occur and how much is needed to reach MTB. Those two benchmarks help establish the health plan's coverage obligations. If no measurable improvement has taken place after undertaking enough therapy to expect to see measurable improvement, coverage can be suspended. Once measurable improvement takes place, coverage will be extended until no further improvement is reported (MTB is reached) and that milestone should occur sometime near the estimated MTB benchmark.

Although medical insurance plans' UM policies are proprietary and not typically published, an online search was undertaken and a UM policy was found from Optum Healthcare Solutions, LLC (Optum).¹⁰ Optum is not a health insurance company but rather a health information technology and services firm that develops programs such as UM policies that can be employed by different medical insurance plans. Optum's Policy 84 "Utilization Management Policy – Determination of Maximum Therapeutic Benefit" describes how a workgroup of clinicians evaluated evidence for various pharmacologic and non-pharmacologic therapies including chiropractic, physical/physio therapy, exercise therapy and acupuncture for the treatment of different neuromusculoskeletal pain conditions.

In the Plain Language summary this policy states:

Most individuals can expect to notice measurable improvement in pain and/or disability early during the course of care – within 2–6 weeks after beginning treatment.

If improvement has not occurred with 6 weeks of treatment, it is highly unlikely that continuing treatment will be helpful.

When initial improvement did occur, many studies showed no additional lasting improvement beyond 6–12 weeks of treatment.

Most flare-ups resolve quickly – within a few days to 3 weeks.

These UM policy findings offer both low-end and high-end averages for the treatment dosage that would likely be required to see the start of measurable benefit and to reach MTB. The high-end estimates suggest that it can take up to six weeks of therapy for the first measurable improvements to occur, 12 weeks of therapy for MTB to be reached and 3 additional weeks of therapy may be needed to resolve flare-ups. While this policy did not detail how many therapy sessions per week would be covered, it is typical in the U.S. for chiropractic therapy, exercise therapy and physical/physio therapy to utilize more than one treatment per week, usually 2–3 sessions per week.

In the design of trials attempting to study acupuncture's effectiveness rates, the issue of the number of treatments needed over what period of time (treatment dose) to either cause some initial measurable benefit or to reach MTB is rarely identified and the rationale for determining the treatment dose is seldom given. This omission suggests that the treatment dose is not viewed as highly important to acupuncture researchers. However, if dose were not important, there would never be a need to perform more than one treatment or for medical insurance plans to bother developing UM policies.

In China, acupuncture treatments are typically administered daily or on alternate days in the first stage of the treatment pro-

cess. Dozens of treatments may be utilized in total, especially in the treatment of chronic conditions. Studies using protocols with ten days of daily treatments constituting "a course of treatment" and utilizing three or more courses (with a few days break in between) are not uncommon. Yet the vast majority of acupuncture trials conducted in the West use far fewer treatments in total and at substantially less frequent intervals, often just one treatment a week.

While there are cultural, social and economic factors that impact how acupuncture is practiced in China vs the West, the significant disparity in treatment dosage deserves scrutiny, especially considering the significant disparity in effectiveness rates often seen in published trials. Could the differences in outcomes reported by studies conducted in China and those conducted in the West reflect factors other than reporting or publication bias? Could factors such as the treatment dose be influencing outcomes? Could it also be that one of the reasons the Chinese trials utilize higher treatment numbers and frequency is that they are routinely attempting to achieve MTB while at least some and perhaps most of the trials conducted in the West are only trying to obtain a limited level of benefit?

The Standards for Reporting Interventions in Controlled Trials of Acupuncture (STRICTA) were developed as an extension of the Consolidated Standards of Reporting Trials (CONSORT) checklist to provide more details of the interventions applied in acupuncture trials.^{11,12} The latest version of STRICTA was published in 2010 and incorporates the following items: 1. Acupuncture rationale, 2. Details of needling, 3. Treatment regimen, 4. Other components of treatment, 5. Practitioner background, 6. Control or comparator interventions.¹² These guidelines touch upon the issue of dose in Item 3 (treatment regimen) which includes the number, duration, and frequency of acupuncture treatments. However, as a trial reporting guideline, no indication is offered as to what an adequate dose of acupuncture may be. There is also no requirement to report if a trial is attempting to measure acupuncture's MTB or a limited benefit.

In their 2008 paper entitled "Defining an adequate dose of acupuncture using a neurophysiological approach - a narrative review of the literature," White et al. attempt to shed some light on the issue of dose.¹³ They reviewed 47 systematic reviews on acupuncture and found only six that considered questions regarding the adequacy of the clinical protocols applied. They quoted one review on knee pain that addressed the issue of treatment frequency and total number over time:

*We defined acupuncture as 'adequate' if it consisted of at least six treatments, at least one per week, with at least four points needled for each painful knee for at least 20 min, and either needle sensation (de qi) achieved in manual acupuncture, or electrical stimulation of sufficient intensity to produce more than minimal sensation."*¹⁴

Perhaps taking their lead from the White et al. paper, at least two subsequent papers addressing treatment dose also supported the notion that a minimum of six treatments constituted an "adequate" dose.^{15,16}

One has to wonder, however, if the concept of an "adequate treatment dose of acupuncture", as mentioned in these papers, is referring to a dose intended to attain MTB or to cause some level of measurable benefit. This is an important issue to clarify because in order to determine any therapy's potential effectiveness rate, one needs to design the study to allow the therapy a reasonable opportunity to achieve its MTB, not just to achieve some initial level of measurable benefit. This is similar to the need in Utilization Management to distinguish between how much of a particular therapy

is needed to allow for measurable improvement to first occur versus how much is needed to reach MTB.

According to the Optum UM policy on determination of MTB, it can take up to six weeks of more than once weekly treatments just to see the first signs of measurable improvement for many pain conditions and up to 12 weeks to reach MTB and that is without any additional treatments to manage flare-ups. While those treatment dosage numbers are lower than those typically used in Chinese clinical practice and research trials, they are higher than treatment numbers used in many Western trials on acupuncture and do not support the notion that six treatments would be adequate when the goal of a trial is to test acupuncture's potential effectiveness rate. In some circumstances, six treatments may not be enough to even cause the first signs of measurable improvement. This is not to suggest that studies using relatively lower dosages of acupuncture have no value. Indeed, there are a number of useful reasons to test the effectiveness of lower treatment dosages. However, individual trials and reviews testing limited applications with lower dosages need to be clearly identified as such and should not be confused with trials or reviews setting out to test acupuncture's potential effectiveness rates (MTB).

Acupuncture trialists' collaboration

Perhaps the best-known review that set out to test acupuncture's potential effectiveness rates was the Acupuncture Trialists' Collaboration (ATC). The ATC conducted an "individual patient data meta-analysis" on acupuncture for chronic pain, with the stated goal of the primary analysis being to "determine the effect size of acupuncture" for chronic pain including acupuncture's specific vs non-specific effect size.¹⁷ The ATC also undertook several secondary analyses of "acupuncture characteristics" from these chronic pain studies including such aspects as the effect sizes seen when comparing the maximum number of sessions allowed, frequency of sessions, durations of sessions, average number of needles used, and minimum years of (acupuncturists') practice required.¹⁸

The ATC first published these findings in 2013 based on the meta-analysis of 17,992 patients from 29 trials and they offered the following thoughts:

"Results: When comparing acupuncture to sham controls, there was little evidence that the effects of acupuncture on pain were modified by any of the acupuncture characteristics evaluated, including style of acupuncture, the number or placement of needles, the number, frequency or duration of sessions, patient-practitioner interactions and the experience of the acupuncturist."

"There is no reason to believe that contemporary acupuncture trials systematically underestimate treatment effects. Though acupuncturists have long been concerned about what constitutes "correct" practice, it can be argued that the consensus methods that are often used to determine acupuncture characteristics - number of treatment sessions, duration of sessions, needle prescriptions, and training and experience of acupuncturists - are appropriate. This is because the variations in outcome associated with these factors are likely to be small."¹⁸

While the ATC's review did not find reason to believe contemporary acupuncture trials systematically underestimate treatment effects, this meta-analysis was limited by the exclusion of studies, such as those done in China, using higher treatment doses. This limitation is acknowledged by the authors:

"nearly 75 % of trials involved between 6 and 15 treatments, and in no trial was acupuncture administered more than twice a week. It is not unusual in China for acupuncture to be given four or five times a week. We were unable to test whether such a level of acupuncture frequency has additional benefit as none of the included primary trials delivered acupuncture this frequently."¹⁸

Not only was the ATC unable to test whether the treatment dosages often employed in China might have caused additional benefits, they were apparently also unable to test if there might be additional benefits from the treatment dosages some U.S. medical insurance plans could be legally compelled to cover as detailed in Optum's UM policy. While no explanation for this was offered, it may have been that the ATC highlighted that 75 % of their selected trials involved between 6 and 15 treatments because the ATC's researchers considered a minimum of 6 treatments to be an adequate dose. But surprisingly, a review of the ATC's patient level data on treatment dose shows a troubling trend with regard to the reporting of treatment dose. While it is true that nearly 75 % of the 29 trials in the ATC review were designed to involve between 6 and 15 treatments, those figures are for the trial level data. A breakdown of the patient level data on treatment dose finds that 48 % of those patients either had their dose listed as not reported (36 %), missing (10 %) or reported as zero treatments (2 %). The actual number of patients that were reported to have had between 6 and 15 treatments was 50 % (39% between 6–10 treatments and 11 % between 11–15 treatments). The ATC published an update of this review in 2018 increasing the total numbers of trials to 39 and patients to 20,827.¹⁹ Again, the patient level data of this updated review showed the same trend; 37 % of treatment sessions not reported, 10 % missing and 2.1 % listed as zero treatments with 38 % of patients getting 6–10 treatments and 10 % getting 11–15 treatments.

It is unfortunate that the ATC were unable to include trials with higher treatment doses although the reason for this is understandable; few trials that satisfy higher standards for the quality of trial design/implementation utilize the higher treatment doses that would better afford acupuncture a chance to achieve MTB. Despite the absence of treatment dose data for nearly half the test subjects, the ATC frequently describes the trials included in their review as "high quality". With barely 10 % of the chronic pain patients in the ATC's review receiving more than 10 treatments, it could be argued that the clinical quality of those trials was sorely lacking. Until it becomes the norm to place as much emphasis on clinical quality as is placed on trial methodology quality, research on acupuncture will risk underestimating that therapy's efficacy and true clinical potential.

Dose in sham-controlled trials

While the ATC's meta-analysis did find a modest improvement in effects size with higher treatment dose when compared to usual care, they did not find this when compared to sham controls. No other aspect of acupuncture research has generated as much controversy as that of sham/placebo controls and the fact that a significant number of Western trials on acupuncture found that verum acupuncture was not superior to sham. Acupuncture critics have, with some degree of success, used these findings to argue against the use of acupuncture, against insurance coverage for acupuncture services and even against the need for acupuncture research.^{20,21} However, little attention has been paid to an interesting trend in some sham controlled studies that

have found sham acupuncture to produce similar outcomes to verum acupuncture when measured at the last treatment, but when measured later at follow-up, significant differences between verum and sham emerged.^{22–24} Three studies in particular; two on osteoarthritis of the knee and one on carpal tunnel syndrome had findings that suggest a possible relationship to treatment dose and also how verum acupuncture compares to sham.^{25–27} All three studies utilized at least two treatments a week for eight weeks but also continued to measure pain relief beyond 12 weeks. While each of these studies found that the pain relief effects of the verum acupuncture and sham acupuncture were not significantly different at week 8, they also found that by week 12 the verum acupuncture's effectiveness had continued to increase while the sham acupuncture's effectiveness had begun to decrease.

Each of these trials found that, after 12 weeks, the verum acupuncture was more effective than sham. Had the trials stopped measuring effectiveness at week 8, they would have been considered “negative” trials adding to the body of evidence suggesting most if not all of acupuncture's observed clinical benefits were due to non-specific/ placebo effects. However, because they kept monitoring the treatment's effects beyond 12 weeks, they all ended up being “positive” trials, adding to the body of evidence that verum acupuncture is more effective than sham.

While these three trials did not set out to test the treatment dosage needed or the time frame of monitoring needed to allow a greater separation between verum and sham acupuncture, the fact that each trial utilized at least 16 treatments over 8 weeks leaves open the possibility that such treatment dosages could better allow verum acupuncture to surpass sham.

The implications of these trials are quite significant. The surprisingly high clinical effectiveness of sham acupuncture could be due to powerful placebo effects as the critics claim or because even sham acupuncture can stimulate the production of the body's natural pain relieving and anti-inflammatory chemistry.^{28–31} However, it could also be that in order to more accurately measure acupuncture's specific vs non-specific effect size, you would need a higher frequency of treatments over a longer duration and continue to monitor progress over a longer period of time than is usually done in Western acupuncture research. In other words, you might need a dose of acupuncture over periods of time closer to those detailed in Optum's UM policies rather than the substantially lower doses typically used in Western research and seen in the ATC's review. How many other trials that found verum acupuncture to not outperform sham may have found otherwise if the study would have utilized more treatments over longer periods of time? Studies investigating this pattern of increasing effectiveness rates for verum vs sham acupuncture and how many treatments over what period of time yield what additional benefits would be most valuable.

Limited benefit vs MTB

“You never know what is enough unless you know what is more than enough.” William Blake: *The Marriage of Heaven and Hell*

In addition to the problem of trials that may have utilized sub-optimal treatment dosages not conducive to attaining MTB, there is evidence that some trials included in reviews attempting to determine potential effect size were never intended to address that issue. Some acupuncture trials set-out to study a limited application of acupuncture to test the potential for a limited outcome and not attempting to attain MBT. However, due to a lack of reporting

guidelines encouraging researchers to clearly identify if they are targeting a limited application vs achieving MTB, these two different types of trials may be inadvertently combined together. Mixing these two different types of trials in reviews can also lead to an underestimation of acupuncture's potential effect size.

This mixing of limited application trials in a review ostensibly trying to estimate acupuncture's maximum effect size appears to have made a pivotal difference in the decision to stop coverage for acupuncture for low back pain by the U.K.'s National Health Service (NHS). In 2016, the National Institute for Health and Care Excellence (NICE) undertook a review of therapies for treating low back pain.³² NICE established a requirement that when compared to sham controls, verum therapies would have to show a “minimum clinically important difference” (MCID) of 1.0 or more on a 0–10 visual analog scale (or equivalent). The difference between acupuncture versus sham was found by NICE to be 0.8, falling just short of the required clinical difference of 1.0, even though it was statistically significant. For this reason, acupuncture was not recommended and was subsequently removed from coverage under the NHS.

Of the 14 sham-controlled trials that met NICE's inclusion criteria, two of those trials used just one acupuncture treatment and one trial used just three.^{33–35} It seems likely that the studies included in NICE's review that used very low numbers of treatments were not designed with the intent to reach MTB. If that was the case, they should not have been included in a review to inform national health insurance policy that set such a firm standard for effect size over sham. Had NICE's review only included studies trying to test the maximum effect size of acupuncture for low back pain, those may have surpassed the MCID of 1.0 over sham and the U.K.'s low back pain sufferers would still be enjoying NHS insurance coverage for acupuncture.

At least one of the trials used in the ATC review was a limited application trial as well. In the ATC's meta-analysis on shoulder pain, one trial clearly intended to test a limited application of acupuncture, not to achieve acupuncture's MTB for shoulder pain.³⁶ This study was testing what is known as a “distal” acu-point; a point a distance away from a painful body part. While distal points are commonly used in acupuncture, they are used less often than “local” points (in and around a painful area). Furthermore, using a single distal point is even less commonplace. The study was comprised of just three treatments over three weeks and used just one point; the ipsilateral distal point Stomach 38, located on the lower leg.

This study found that the use of this single distal point provided a statistically significant improvement and concluded:

“Single-point acupuncture in association with physiotherapy improves shoulder function and alleviates pain, compared with physiotherapy as the sole treatment. This improvement is accompanied by a reduction in the consumption of analgesic medicaments.”

However, in the section detailing “Methodological limitations”, the study's authors added this caveat:

“Although this study shows the single-point acupuncture technique to be effective, it is probable that a selection combining the use of distal and local acupuncture points would have improved results still further, and widened the differences between the two groups.”

This statement makes clear that the study's authors were not intending this study as one to investigate acupuncture's maximum possible effect size but rather to test a limited application of acupuncture that would likely produce a less robust effect size. Unfortunately, the statement indicating this is found at the end of the study and not reflected in the abstract. While the study's

authors did not mention the low number of treatments used (3) nor indicate that using more treatments might have also produced higher effectiveness rates, it is likely the authors would have thought this at least possible.

This single needle study for shoulder pain could not be labeled as a “false negative” because it ended-up finding acupuncture to be effective. However, if the study’s authors were correct in their belief that utilizing both local and distal points would have produced a higher effect size, its inclusion in the ATC means it produced a less significant positive than it could have. In fact, this study yielded the lowest effect size out of the three studies included in the ATC’s sham-controlled review for shoulder pain. Also, as this trial had the largest number of test subjects of the included trails, it was the most heavily weighted. In other words, the average effect size of acupuncture for shoulder pain reported by the ATC was lower than it could have been, had the ATC excluded trials not attempting to reach MTB.

Another example of a trial testing a limited application of acupuncture that seemed to conflate their limited application protocol as one testing MTB is a 2017 study “Sham acupuncture is as efficacious as true acupuncture for the treatment of IBS: A randomized placebo controlled trial”.³⁷ This study employed 2 treatments a week for 4 weeks and repeatedly states that they found that real acupuncture was not superior to sham. In the Abstract Conclusions & Inferences they state flatly that “The lack of differences in symptom outcomes between sham and true treatment acupuncture suggests that acupuncture does not have a specific treatment effect in IBS.”

However, near the end of the study, the authors point to this actually being a limited application study when they stated “Our analysis was not intent-to-treat, but we feel that the per-protocol presented more appropriately addressed the question which is not whether acupuncture is effective but whether a 4 week true acupuncture treatment provides benefits compared to a 4 week sham acupuncture treatment.”

It is commendable that this study’s authors attempted to clarify that this study was not one to address if acupuncture is effective for IBS but rather if the limited dose they employed – 8 treatments over 4 weeks – was found to be superior to sham. Unfortunately, one would not understand this distinction by looking at the study’s title or reading the abstract or even the conclusion. One would have to read the entire study to find this clarification. If a review of acupuncture’s effectiveness in treating IBS were to be undertaken, there is a chance this trial might be mistakenly included. How many acupuncture trials, including those selected in well-meaning reviews, are of a similar nature; limited application trials being mistaken for ones attempting to test acupuncture’s full potential? Studies investigating this question would also be very helpful.

Examples of higher effectiveness with higher treatment dosages

The following is a brief description of a collection of studies that found higher effectiveness rates for acupuncture when higher treatment dosages were used and is offered as further evidence that there is sufficient reason to believe that many acupuncture trials are utilizing suboptimal treatment dosages that can lead to suboptimal clinical results. This is not intended as a comprehensive review of the body of acupuncture research and some may find fault with the conclusions some of these studies reached.

A Cochrane systematic review on acupuncture for migraine prophylaxis performed a subgroup analysis on the number of treatment sessions given.¹⁵ When the effect sizes for response and headache frequency reduction (both after treatment and at follow-

up) were compared, 16 treatments or more produced almost double the effect sizes compared to 12 treatments or fewer, in all four outcomes.

In a review of RCTs on acupuncture for allergic rhinitis, all trials which delivered at least 12 treatments at a frequency of at least twice weekly, consistently demonstrated significant differences (both statistically and clinically) between verum and sham acupuncture, while those trials using less than 12 treatments or less frequent treatments did not.³⁸

A recent systematic review specifically examining the effect of acupuncture treatment dose on outcomes in knee osteoarthritis, found that: “Compared with LD [low dosage] and MD [medium dosage] acupuncture treatments, strong evidence showed that there was a positive correlation between HD [high dosage] acupuncture treatment and positive outcomes”.³⁹

A recent systematic review and meta-analysis on acupuncture for depression concluded that “both the total number of treatments and the frequency of treatment may play a role in depression-related outcomes”.⁴⁰

A review of 33 RCTs published in 2015 studied the “negative results of international clinical trials on acupuncture”. The authors cited several possible clinical reasons for why some studies found negative results vs positive results including poor point selection and acupuncturists training. They also cited “acupuncture treatment frequency [is] too low in most studies” and stated “Indeed, the studies with positive results had a significantly higher treatment frequency”.³

An important question in acupuncture practice and in research is: “How many treatments, with what frequency, and over what period of time are required to allow acupuncture to be as effective as it could be?” The current evidence suggests that, in general, six treatments at once a week may not be sufficient and that two or more treatments a week for six to twelve weeks would be a more reliable dose, at least for chronic pain. However, even studies using that dose would need longer-term follow up than is generally employed, in order to capture delayed effects and lasting modulations.

A closely related issue that must also be addressed is whether or not any given trial is meant to test a limited application of acupuncture or to test its potential maximum therapeutic benefit (MTB). This needs to be clearly stated in trial reporting to enable systematic reviews and meta-analyses to separate the two types of trials.

Limitations

The acupuncture research which has been discussed in this paper was mainly relevant to chronic pain conditions and chronic inflammatory conditions. From these studies it appears that there may be a minimum threshold to produce statistically and clinically significant differences at the highest possible rates, for example a minimum of 12 treatments twice weekly for allergic rhinitis or 16 treatments twice weekly for chronic pain. However, more research and clinical expert consensus building processes are needed to determine what is optimal treatment frequency and duration, and this may vary for every condition or patient treated. When translating this research into clinical practice, each practitioner must then adapt such broad guidelines to the needs of each individual patient. Fortunately, creating individualized treatments has always part of acupuncture’s millennia-old tradition.

Recommendations

Members of the acupuncture research community need to acknowledge that in order for trials to generate reliable evidence

regarding acupuncture's potential effectiveness, steps must be taken to ensure the verum acupuncture is afforded a chance to achieve MTB and justification of these steps needs to be described.

If a trial is not intended to gauge acupuncture's MTB but rather to test a limited application of acupuncture techniques, this needs to be clearly stated in the title and/or description of the research when published and STRICTA should add this as a reporting requirement under Item 1. Acupuncture rationale.

Experienced acupuncture clinicians need to work at developing best practice clinical quality guidelines to guide both researchers and clinicians to reach, at the very least, an understanding of how many treatments, over what period of time, acupuncture therapy may need to be applied to achieve MTB.

Until such time that best practice clinical quality guidelines can be established to guide both future acupuncture research and systematic reviews of acupuncture trials, panels of clinical experts should be formed and used to guide researchers in understanding how to distinguish optimal from suboptimal clinical quality protocols to reduce the number of poor clinical quality RCTs and foster more accurate analysis and sub-analysis in systematic reviews.

To help guide future research and clinical practice, more systematic reviews/meta-analyses of existing acupuncture trials should be undertaken with sub-group analysis to measure the influence of different factors on clinical outcomes. These should include (but are not limited to) treatment frequency, total number of treatments, and the training and experience of acupuncturists involved in the study design and the delivery of the intervention.

Author contributions

Matthew Bauer and John McDonald were the two principle authors while Natalie Chandra Saunders was involved in writing the first draft and later edited and corrected the manuscript,

Conflict of interest

The authors declare no conflict of interest.

Funding

Acupuncture Now Foundation provided some funding for the writing and editing of this article.

Ethical statement

No Human Research Ethics Committee approval was required as no human research was conducted.

Data availability


All sources have been cited and no new data is presented.

References

- Langevin HM, Wayne PM, Macpherson H, et al. Paradoxes in acupuncture research: Strategies for moving forward. *Evid Based Complement Alternat Med* 2011;2011:180805.
- Ernst E, Edzard Ernst Website <https://edzardernst.com/2014/05/and-this-is-why-we-might-as-well-forget-about-chinese-acupuncture-trials/>. Published 2014 Accessed October 5 *And this is why we might as well forget about Chinese acupuncture trials*; 2019.
- Liu WH, Hao Y, Han YJ, Wang XH, Li C, Liu WN. Analysis and thoughts about the negative results of international clinical trials on acupuncture. *Evid Based Complement Alternat Med* 2015;2015:671242.
- Birch S. A review and analysis of placebo treatments, placebo effects, and placebo controls in trials of medical procedures when sham is not inert. *J Altern Complement Med* 2006;12(3):303–10.
- Linde K, Niemann K, Schneider A, Meissner K. How large are the nonspecific effects of acupuncture? A meta-analysis of randomized controlled trials. *BMC Med* 2010;8:75.
- Lund I, Naslund J, Lundeberg T. Minimal acupuncture is not a valid placebo control in randomised controlled trials of acupuncture: A physiologist's perspective. *Chin Med-UK* 2009;4:1.
- White AR, Filshie J, Cummings TM. Clinical trials of acupuncture: Consensus recommendations for optimal treatment, sham controls and blinding. *Complement Ther Med* 2001;9(4):237–45.
- White PJ. Methodological concerns when designing trials for the efficacy of acupuncture for the treatment of pain. *Adv Exp Med Biol* 2004;546:217–27.
- Deng S, Zhao X, Du R, et al. Is acupuncture no more than a placebo? Extensive discussion required about possible bias. *Exp Ther Med* 2015;10(4):1247–52.
- OptumHealth Physical Health, <https://www.myoptumhealthphysicalhealth.com/ClinicalPolicies/84.pdf>. Published April 25, 2019 Accessed November 20 *Utilization management policy. OptumHealth physical health website*; 2019.
- MacPherson H, Altman DG, Hammerschlag R, et al. Revised STAndards for reporting interventions in clinical trials of acupuncture (STRICTA): Extending the CONSORT statement. *Aust J Acupunct Chinese Med* 2010;5(2):8–22.
- Altman DG, Schulz KF, Moher D, et al. The revised CONSORT statement for reporting randomized trials: Explanation and elaboration. *Ann Intern Med* 2001;134(8):663–94.
- White A, Cummings M, Barlas P, et al. Defining an adequate dose of acupuncture using a physiological approach - a narrative review of the literature. *Acupunct Med* 2008;26(2):111–20.
- White A, Foster NE, Cummings M, Barlas P. Acupuncture treatment for chronic knee pain: A systematic review. *Rheumatology* 2007;46(3):384–90.
- Linde K, Allais G, Brinkhaus B, et al. Acupuncture for the prevention of episodic migraine. *Cochrane Database Syst Rev* 2016;(6):Cd001218.
- Vincent CA. A controlled trial of the treatment of migraine by acupuncture. *Clin J Pain* 1989;5(4):305–12.
- Vickers AJ, Cronin AM, Maschino AC, et al. Acupuncture for chronic pain: Individual patient data meta-analysis. *Arch Intern Med* 2012;172(19):1444–53.
- MacPherson H, Maschino AC, Lewith G, Foster NE, Witt CM, Vickers AJ. Characteristics of acupuncture treatment associated with outcome: An individual patient meta-analysis of 17,922 patients with chronic pain in randomised controlled trials. *PLoS One* 2013;8(10):e77438.
- Vickers AJ, Vertosick EA, Lewith G, et al. Acupuncture for chronic pain: Update of an individual patient data meta-analysis. *J Pain* 2017.
- MacLennan AH, Morrison RG. Tertiary education institutions should not offer pseudoscientific medical courses. *Med J Aust* 2012;196(4):225–6.
- Friends of Science in Medicine, Friends of Science in Medicine Website <https://www.scienceinmedicine.org.au/> Published 2016. Accessed October 5, *Is there any place for acupuncture in 21st century medical practice?*; 2019.
- McDonald JL, Smith PK, Smith CA, Xue CC, Golianu B, Cripps AW. Effect of acupuncture on house dust mite specific IgE, substance P, and symptoms in persistent allergic rhinitis. *Ann Allergy Asthma Immunol* 2016;116(6):497–505.
- Brinkhaus B, Ortiz M, Witt CM, et al. Acupuncture in patients with seasonal allergic rhinitis: A randomized trial. *Ann Intern Med* 2013;158(4):225–34.
- Xue CC, An X, Cheung TP, et al. Acupuncture for persistent allergic rhinitis: A randomised, sham-controlled trial. *Med J Aust* 2007;187(6):337–41.
- Berman BM, Lao L, Langenberg P, Lee WL, Gilpin AM, Hochberg MC. Effectiveness of acupuncture as adjunctive therapy in osteoarthritis of the knee: A randomized, controlled trial. *Ann Intern Med* 2004;141(12):901–10.
- Miller E, Maimon Y, Rosenblatt Y, et al. Delayed effect of acupuncture treatment in OA of the knee: A blinded, randomized, controlled trial. *Evid Based Complement Alternat Med* 2011;2011:792975.
- Maeda Y, Kim H, Kettner N, et al. Rewiring the primary somatosensory cortex in carpal tunnel syndrome with acupuncture. *Brain* 2017;140(4):914–27.
- McDonald JL, Cripps AW, Smith PK. Mediators, receptors, and signalling pathways in the anti-inflammatory and antihyperalgesic effects of acupuncture. *Evid Based Complement Alternat Med* 2015;2015:975632.
- McDonald JL, Cripps AW, Smith PK, Smith CA, Xue CC, Golianu B. The anti-inflammatory effects of acupuncture and their relevance to allergic rhinitis: A narrative review and proposed model. *Evid Based Complement Alternat Med* 2013;2013:591796.
- Chen S, Wang S, Rong P, et al. Acupuncture for visceral pain: Neural substrates and potential mechanisms. *Evid Based Complement Alternat Med* 2014;2014:609594.
- Zhang R, Lao L, Ren K, Berman BM. Mechanisms of acupuncture-electroacupuncture on persistent pain. *Anesthesiology* 2014;120(2):482–503.
- National Institute for Health and Care Excellence (NICE), NICE Website <https://www.nice.org.uk/guidance/ng59> Published November 2016 Accessed December 14 *Low back pain and sciatica in over 16s: Assessment and management*; 2019.

33. Shin JS, Ha IH, Lee J, et al. Effects of motion style acupuncture treatment in acute low back pain patients with severe disability: A multicenter, randomized, controlled, comparative effectiveness trial. *Pain* 2013;154(7):1030–7.
34. Inoue M, Kitakoji H, Ishizaki N, et al. Relief of low back pain immediately after acupuncture treatment—a randomised, placebo controlled trial. *Acupunct Med* 2006;24(3):103–8.
35. Edelist G, Gross AE, Langer F. Treatment of low back pain with acupuncture. *Can Anaesth Soc J* 1976;23(3):303–6.
36. Vas J, Ortega C, Olmo V, et al. Single-point acupuncture and physiotherapy for the treatment of painful shoulder: A multicentre randomized controlled trial. *Rheumatology* 2008;47(6):887–93.
37. Lowe C, Aiken A, Day AG, Depew W, Vanner SJ. Sham acupuncture is as efficacious as true acupuncture for the treatment of IBS: A randomized placebo controlled trial. *Neurogastroenterol Motil* 2017;29(7).
38. McDonald JL. *The effects of acupuncture on mucosal immunity in the upper respiratory tract [PhD thesis]. Gold Coast, Queensland, Australia: Griffith University; 2014.*
39. Sun N, Tu JF, Lin LL, et al. Correlation between acupuncture dose and effectiveness in the treatment of knee osteoarthritis: A systematic review. *Acupunct Med* 2019;37(5):261–7.
40. Armour M, Smith CA, Wang LQ, et al. Acupuncture for depression: A systematic review and meta-analysis. *J Clin Med* 2019;8(8):1140.

Matthew Bauer^a

John Leslie McDonald ^{b,*}

Natalie Saunders^a

^a *Acupuncture Now Foundation, Queensland, Australia*

^b *School of Medicine, Griffith University, Queensland, Australia*

* Corresponding author at: 5 Quartz Place, Carrara, Qld, 4211, Australia.

E-mail address: twindragon@bigpond.com
(J.L. McDonald)

15 October 2019

Available online 20 January 2020