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A Rumsfeld Matrix test for acupuncture clinical trials

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ABSTRACT

This study examined the application of the Rumsfeld Matrix to acupuncture clinical trials, particularly those published in leading medical journals such as *The Journal of the American Medical Association* (JAMA), *British Medical Journal* (BMJ), *The Lancet*, and *The New England Journal of Medicine* (NEJM). The integration of randomized clinical trials (RCTs) has introduced a level of academic rigor to acupuncture research, challenging the classical deterministic model and revealing a complex landscape of known knowns, known unknowns, unknown knowns, and unknown unknowns. While RCTs have validated acupuncture's efficacy in certain conditions, they have also highlighted considerable challenges, including the limitations of control group designs and the potential influence of placebo effects. The recurring issue of no significant differences between real and sham acupuncture in many studies underscores the need for refined control strategies and a more nuanced understanding of acupuncture's mechanisms. This investigation calls for continued rigorous research to fully explore acupuncture's therapeutic potential and its integration into evidence-based medicine, ultimately contributing to improved patient care and broader acceptance within the medical community.

1 Introduction

In the classical deterministic acupuncture model, there is a presumption of absolute certainty. This model operates on the belief that outcomes are predictable and repeatable, without any room for variation or unpredictability. Such viewpoints have traditionally guided the practice of acupuncture, providing a sense of reliability and consistency in treatment outcomes. However, this deterministic approach often falls short in addressing the complexities and variabilities inherent in human health and medical treatments, which assumes a linear cause-and-effect relationship that does not account for the myriad of factors influencing individual health responses.

The introduction of randomized clinical trials (RCTs) into acupuncture research has revolutionized the field by incorporating a layer of academic rigor and validation. RCTs are considered the gold standard in clinical research because they minimize bias, control for confounding variables, and provide a high level of evidence for the efficacy and safety of treatments. By applying RCTs to acupuncture, researchers can systematically evaluate its therapeutic efficacy, compare it to placebos or other treatments, and ultimately validate or refute its clinical benefits. This scientific methodology not only promotes the credibility of acupuncture, but also paves the way for a more nuanced understanding of its mechanisms and applications.

The famous quote by Donald Rumsfeld, "As we know, there are known knowns; there are things we know we

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know. We also know there are known unknowns; that is to say, we know there are some things we do not know. But there are also unknown unknowns — the ones we don't know we don't know", aptly captures the essence of scientific exploration and discovery. To complete the Rumsfeld Matrix, we need to include "unknown knowns", which are elements that we are unaware that we know — often buried in our subconscious minds, overlooked, or dismissed as irrelevant. As shown in Table 1, the Rumsfeld Matrix is defined by four quadrants that categorizes information into types: known knowns, known unknowns, unknown knowns, and unknown unknowns [1]. In the context of clinical trials in acupuncture, RCTs act as a critical tool in navigating these different levels of knowledge which substantially serves clinical practice. RCTs play a beneficial role in assisting professionals delineate the "known knowns" by confirming established facts and treatment outcomes that are consistent and reproducible. For instance, RCTs can validate that acupuncture effectively alleviates certain types of pain, which becomes a "known known". Moreover, RCTs illuminate the "known unknowns" by identifying areas where current knowledge is insufficient or uncertain. For example, while acupuncture might be known to provide pain relief, the specific physiological mechanisms behind this effect remain to be fully elucidated. RCTs can thus guide further research to explore these unknowns, leading to deeper insights and advancements in the field. "Unknow knows" displays the overlooked or unconsciously accepted facts from the RCTs. Additionally, the systematic approach of RCTs can reveal "unknown unknowns", unexpected findings that were not previously considered. These findings can open new avenues for research and expand the understanding of acupuncture's potential applications and limitations.

Table 1 Rumsfeld Matrix

Knowledge type	Characteristic
Known knowns	Things that are understood and recognized
Unknown knowns	Things that are understood but not recognized
Known unknowns	Things that are recognized but not understood
Unknown unknowns	Things that are neither recognized nor understood

The integration of RCTs into acupuncture research represents a marked advancement from the traditional deterministic model, which embraces the complexity and uncertainty inherent in medical sciences, allowing for a more robust and comprehensive exploration of acupuncture's efficacy and mechanisms. Professionals can navigate the landscape of "known knowns, known unknowns, unknown knowns, and unknown unknowns" via RCTs, ultimately contributing to a more informed and evidence-based practice of acupuncture.

2 Acupuncture RCTs in four renown medical journals

By February 2022, the number of RCTs focused on acupuncture had surged to an enormous 14 000 [2], laying the foundation for over 2 400 systematic reviews and meta-analyses [3], which in turn contributed to the development of over 130 clinical practice guidelines [4]. This burgeoning volume of research continues to grow at an accelerating pace, demonstrating the increasing interest and investment in understanding the clinical efficacy of acupuncture. The rapid expansion of RCTs has led to a major presence of high-quality studies published in prestigious medical journals across various fields. Notably, these studies were not confined to niche publications but were featured prominently in some of the most respected clinical medical journals worldwide, highlighting the broad relevance and acceptance of acupuncture research in the medical community.

In this paper, we have selected all acupuncture RCTs published in four of the most esteemed medical journals: *The Journal of the American Medical Association* (JAMA), *British Medical Journal* (BMJ), *The Lancet,* and *The New England Journal of Medicine* (NEJM) (Table 2). These journals are renowned for their rigorous peer-review processes and high standards for scientific quality and clinical relevance. By focusing on these publications, we aim to examine a representative sample of acupuncture RCTs that demonstrate the highest level of research integrity and impact. Although this selection represents a relatively small subset of the total number of RCTs in acupuncture, it encapsulates the critical issues and findings that characterize the broader population of acupuncture research.

This collection of 34 RCTs [5-38] provides a comprehensive examination of acupuncture's efficacy across various conditions. These studies encompass a wide range of diseases, from chronic pain and osteoarthritis to asthma and chemotherapy-induced nausea, which adopted rigorous methodological designs, including single-blind and double-blind protocols.

Key findings from these studies reveal a complex picture of acupuncture's efficacy. In some cases, such as the treatment of chemotherapy-induced nausea [19] and joint pain in breast cancer patients [36], acupuncture was found to be superior to sham treatments, suggesting potential therapeutic benefits. However, many studies, particularly those exploring chronic pain [5, 18], knee osteoarthritis [33], and neuropathic pain in human immunodeficiency virus (HIV) patients [18], reported no significant difference between real and sham acupuncture, raising questions about the specific mechanisms at play and the role of placebo effects.

These RCTs also highlight the challenges in acupuncture research, particularly in designing appropriate control groups. The frequent use of superficial needling or

Table 2 RCTs published by the top four medical journals

First author & year of publication	Journal	Disease	Sample size	Study design	Treatment group	Control group	Outcome comparison
LEE, 1975 [5]	JAMA	Chronic pain	261	Controlled observation	Standard acupoints	Random acupoints	No difference between real and sham acupoints
GAW, 1975 [6]	NEJM	Arthritis	40	Single-center, randomized, double-blind	Standard acupoints, traditional Chinese acupuncture	Non-traditional acupoint needling	No significant difference between real and sham acupuncture
SJÖLUND, 1976 [7]	*The Lancet*	Pain	29	Randomized, controlled, double-blind	Transcutaneous electrical stimulation + naloxone	Transcutaneous electrical stimulation + saline	Transcutaneous electrical stimulation produces endogenous morphine-like substances
STEWART, 1977 [8]	BMJ	Pain	12	Two-group control	Hegu, Zusanli electroacupuncture	Non-acupoint electroacupuncture	No significant difference between groups
CAHN, 1978 [9]	*The Lancet*	Pain during endoscopy	90	Randomized, controlled, double-blind	Standard acupoints, traditional Chinese acupuncture	1 cm from the treatment group acupoints	Standard acupoint group superior to non-classical acupoint group
FERNANDES, 1980 [10]	*The Lancet*	Rotator cuff syndrome	60	Randomized, controlled	Standard acupoints, traditional Chinese acupuncture	Methylprednisolone injection; corticosteroid injection + tolmetin sodium; physiotherapy; sham tolmetin sodium + sham physiotherapy	No significant difference among the five groups
ABBATE, 1980 [11]	*The Lancet*	Pain management after thoracic surgery	12	Randomized, controlled	Electroacupuncture ear acupoints + small dose anesthetic	Large dose anesthetic	Electroacupuncture group required no additional painkillers, and endorphins activated
FUNG, 1986 [12]	*The Lancet*	Asthma	19	Randomized, controlled, single-blind	Real acupuncture	Sham acupuncture	Significant difference between real and sham acupuncture
JOBST, 1986 [13]	*The Lancet*	Disabling dyspnea	26	Randomized, controlled	Standard acupoints, traditional Chinese acupuncture	Non-standard acupoints	Significant difference in subjective indicators; no significant difference in objective indicators
DUNDEE, 1987 [14]	*The Lancet*	Vomiting response to cisplatin chemotherapy	10	Randomized, controlled	Electroacupuncture Neiguan	Electroacupuncture adjacent non-acupoint	Significant difference between groups
BULLOCK, 1989 [15]	*The Lancet*	Severe chronic alcoholism	80	Randomized, controlled	Electroacupuncture NADA acupoints	Within 5 mm of NADA acupoints	Significant difference between groups
DELUZE, 1992 [16]	BMJ	Fibromyalgia syndrome	70	Multicenter, Randomized, controlled	Electroacupuncture at four common acupoints	Sham acupuncture	Real acupuncture superior to sham acupuncture
CARDINI , 1998 [17]	JAMA	Breech presentation	260	Multicenter, randomized, controlled, single-blind	Standard acupoints, moxibustion	Conventional treatment, no moxibustion	Moxibustion superior to conventional treatment
SHLAY, 1998 [18]	JAMA	Peripheral neuropathy in HIV patients	250	Multicenter, randomized, controlled, single-blind	Standard acupoints, traditional Chinese acupuncture	Superficial needling, non-acupoints, same stimulation	No statistical difference between real and sham acupuncture
SHEN, 2000 [19]	JAMA	Nausea and vomiting after chemotherapy	104	Randomized, controlled, single-blind	Standard acupoints, low-frequency electroacupuncture	Minimal needling	Real acupuncture superior to sham acupuncture

Table 2 Continued

First author & year of publication	Journal	Disease	Sample size	Study design	Treatment group	Control group	Outcome comparison
IRNICH, 2001 [20]	BMJ	Chronic neck and shoulder pain	177	Multicenter, randomized, controlled	Acupuncture	Massage, laser acupuncture	No significant difference between acupuncture and laser acupuncture
MARGOLIN, 2002 [21]	JAMA	Cocaine addiction	620	Multicenter, randomized, controlled, single-blind	Standard ear acupoints	One needle or relaxation training	No statistical difference between groups
VICKERS, 2004 [22]	BMJ	Chronic headache	401	Multicenter, randomized, controlled	Traditional Chinese acupuncture + conventional treatment	Conventional treatment	Significant difference between groups
VAS, 2004 [23]	BMJ	Knee osteoarthritis	97	Single-center, randomized, single-blind	Standard acupoints, traditional Chinese acupuncture	Standard acupoints, no penetration	Real acupuncture superior to sham acupuncture on the basis of diclofenac potassium
MELCHART, 2005 [24]	BMJ	Tension headache	270	Multicenter, randomized, controlled	Standard acupoints, traditional Chinese acupuncture	Non-acupoint superficial needling or waiting	No significant difference between traditional chinese acupuncture and non-acupoint superficial needling
ELDEN, 2005 [25]	BMJ	Pelvic pain	386	Multicenter, randomized, controlled	Acupuncture + conventional treatment	Conventional treatment or conventional treatment + exercise	Significant difference between acupuncture plus conventional treatment and conventional treatment alone
WITT, 2005 [26]	*The Lancet*	Knee osteoarthritis	294	Multicenter, randomized, single-blind	Standard acupoints, traditional Chinese acupuncture, trigger points	Superficial needling, non-acupoints, no stimulation	Real acupuncture superior to sham acupuncture
LINDE, 2005 [27]	JAMA	Neurogenic headache	302	Multicenter, randomized, controlled, single-blind	Standard acupoints, traditional Chinese acupuncture	Superficial needling, non-acupoints, no stimulation	No statistical difference between real and sham acupuncture
THOMAS, 2006 [28]	BMJ	Non-specific low back pain	241	multicenter, randomized, controlled	Standard acupoints, traditional Chinese acupuncture	Conventional treatment	No significant difference in short-term, but a significant difference in long-term
KAPTCHUK, 2006 [29]	BMJ	Arm pain	270	Randomized, controlled	Sham acupuncture	Placebo pill	Sham acupuncture more effective than placebo pills
FOSTER, 2007 [30]	BMJ	Osteoarthritis of the knee	352	Multicenter, randomized, single-blind	Standard acupoints, traditional Chinese acupuncture, trigger points	Standard acupoints, no penetration	No significant difference between real and sham acupuncture plus physiotherapy
KAPTCHUK, 2008 [31]	BMJ	Irritable bowel syndrome	262	Single-blind, three-arm randomized controlled trial	Placebo acupuncture + care	Placebo acupuncture or waiting	Placebo acupuncture plus care superior to placebo acupuncture
WECHSLER, 2011 [32]	NEJM	Asthma	39	Experimental, crossover study	Salbutamol inhaler	Sham acupuncture control	No significant difference between drug inhalation and sham acupuncture
HINMAN, 2014 [33]	JAMA	Knee osteoarthritis	282	Multicenter, randomized, controlled, single-blind	Standard acupoints, traditional Chinese acupuncture	Laser acupuncture, sham laser acupuncture	No significant difference between real and sham acupuncture

Table 2 Continued

First author & year of publication	Journal	Disease	Sample size	Study design	Treatment group	Control group	Outcome comparison
LIU, 2017 [34]	JAMA	Stress urinary incontinence	504	Multicenter, randomized, controlled, single-blind	Standard acupoints, traditional Chinese acupuncture, electroacupuncture	Sham electroacupuncture, non-acupoints, no skin penetration	Real acupuncture superior to sham acupuncture
WU, 2017 [35]	JAMA	Ovulation in polycystic ovary syndrome	1 000	Multicenter, randomized, controlled, single-blind	Standard acupoints, traditional Chinese acupuncture	Superficial needling, non-acupoints, no stimulation	No statistical difference between real and sham acupuncture
HERSHMAN, 2018 [36]	JAMA	Joint pain in breast cancer patients	226	Multicenter, randomized, controlled, single-blind	Standard acupoints, traditional Chinese acupuncture	Superficial needling, non-acupoints, minimal penetration	Real acupuncture superior to sham acupuncture
SMITH, 2018 [37]	JAMA	IVF success rate	848	Multicenter, randomized, controlled, single-blind	Standard acupoints, traditional Chinese acupuncture	No penetration, non-acupoints, no stimulation	No statistical difference between real and sham acupuncture
XU, 2020 [38]	BMJ	Prophylactic treatment of migraine without aura	150	Multicenter, randomized, single-blind	Filiform needle + conventional treatment	Non-penetrating sham acupuncture, applied to non-acupoints in heterogeneous segments	Filiform needle superior to sham acupuncture

non-acupoint stimulation as controls may inadvertently trigger biological responses, complicating the interpretation of results. Despite these challenges, these studies have demonstrated the potential for acupuncture to complement conventional treatments, particularly in areas such as obstetrics [17] and addiction [15]. This body of research highlights the need for continued methodological refinement and further investigation to clarify the conditions under which acupuncture is most effective and to better understand its mechanisms of action.

Despite being a fraction of the overall body of RCTs in acupuncture, the studies published in these prestigious journals hold considerable sway in the medical research community, which were frequently referenced and widely cited, exerting influence on clinical guidelines, policy decisions, and the direction of further research. Besides, these RCTs are typically designed and conducted with meticulous attention to methodological rigor, addressing potential biases and confounding factors to the largest extent possible. This level of scrutiny ensures that the findings are robust, reliable, and generalizable to wider clinical practice.

However, these high-quality RCTs also highlight common challenges and issues prevalent across the entire spectrum of acupuncture research. For instance, variability in study designs, differences in patient populations, and the diversity of acupuncture techniques can complicate the interpretation and comparison of results. Additionally, the subjective nature of some outcome measures, such as pain relief and patient-reported outcomes, can introduce a degree of variability that is challenging for standardization. These issues highlight the importance of continued methodological refinement and standardization in acupuncture research to raise the reliability and applicability of findings.

2.1 Known knowns (well-established facts where the trials show consistent specific outcomes)

Numerous studies have demonstrated that acupuncture is superior to no treatment and, in some cases, to standard conventional treatments. This is particularly important given the growing adoption of acupuncture as a complementary therapy in modern medical practice. For conditions such as pain management, patients receiving acupuncture reported notable reductions in pain levels compared with those without intervention. This benefit is supported by a substantial body of evidence from well-designed RCTs. The consistent findings from research and clinical observations underscore acupuncture's value as an effective therapeutic option, with its role likely to expand as interest in integrative and holistic health approaches grows, which enhances patients' overall treatment experiences and outcomes.

Acupuncture has shown consistent and reproducible benefits in specific medical conditions where objective physiological outcomes can be measured. For example, CARDINI et al. [17] found that add-on moxibustion was superior to conventional treatments for correcting breech presentation in pregnancy. SHEN et al. [19] demonstrated that low-frequency electroacupuncture significantly alleviated nausea and vomiting in chemotherapy patients compared to minimal needling. LIU et al. [34] also reported that real acupuncture outperformed sham acupuncture in treating stress urinary incontinence.

These findings suggest that acupuncture is highly effective in conditions with clear and measurable physiological responses.

Several trials strongly demonstrate well-established outcomes for acupuncture's effectiveness in specific conditions. DELUZE's 1992 study [16] on fibromyalgia syndrome found that real electroacupuncture significantly outperformed sham acupuncture. VICKERS' 2004 research [22] on chronic headaches showed that acupuncture combined with conventional treatment provided significant benefits over conventional treatment alone. Similarly, DUNDEE's 1987 study [14] on the vomiting response to cisplatin chemotherapy indicated that electroacupuncture significantly decreased vomiting compared to non-acupoint stimulation. BULLOCK's 1989 trial [15] on severe chronic alcoholism also demonstrated that electroacupuncture targeting NADA points was significantly more effective than control treatments. Moreover, WITT's 2005 study [26] of knee osteoarthritis found that real acupuncture outperformed sham acupuncture. These results reinforce acupuncture's therapeutic value in these areas.

The comparison between acupuncture and standard conventional treatment often shows that acupuncture can act as an effective alternative or adjunctive therapy. For instance, acupuncture has consistently shown promising results in the management of chronic pain conditions such as osteoarthritis or lower back pain. Studies have indicated that patients receiving acupuncture experience greater pain relief and functional improvement compared with those who underwent conventional treatments such as physical therapy or medication. This suggests that acupuncture may offer unique benefits that standard treatments do not provide, possibly due to its holistic approach to patient care, which addresses both physical and psychological aspects of pain.

Furthermore, the clinical efficacy of acupuncture observed in research is in line with the experiences of practitioners and patients in real-world settings. Clinicians who integrate acupuncture into their practice often report positive outcomes, such as reduced symptom severity and improved patient's degree of satisfaction. Patients frequently report a preference for acupuncture over conventional treatments, citing not only the relief of their symptoms but also the overall sense of well-being and relaxation they experience during and after sessions. This anecdotal evidence from clinical practice provides additional support for the findings of controlled studies, strengthening the credibility and reliability of acupuncture as a therapeutic modality.

The consistency between research findings and clinical observations also highlights the potential of acupuncture to fill gaps in conventional medical treatments. For conditions where standard treatments are either insufficiently effective or associated with undesirable side effects, acupuncture serves as a promising alternative. For instance, acupuncture has been found to be more effective than conventional anti-nausea medications for some patients in treating chemotherapy-induced nausea and vomiting. This effectiveness not only promotes patient comfort and quality of life but also supports the overall treatment regimen by enabling patients to adhere strictly to their chemotherapy schedules.

Moreover, the holistic approach of acupuncture, involving the stimulation of specific points on the body to promote natural healing processes, may contribute to its effectiveness across various conditions. This approach contrasts sharply with conventional treatments that often focus on isolated symptoms or specific disease mechanisms. By addressing the body as an interconnected system, acupuncture can potentially offer broader therapeutic benefits, including improved mental health, strengthened immune function, and promoted overall resilience against illness.

In conditions where outcomes are more subjective, such as chronic pain, neurogenic headaches, and peripheral neuropathy, acupuncture has shown less significant differences compared with sham treatments. Multiple RCTs have demonstrated no significant difference between real acupuncture and sham acupuncture in these conditions. Both real and sham acupuncture involves needle insertion, but sham acupuncture typically uses more superficial needling at non-traditional points, generating a less intense but still perceptible sensation. LEE's 1975 study [5] of chronic pain found no significant difference between real and sham acupuncture, raising important questions about the mechanisms behind acupuncture's pain relief. Similarly, SHLAY's 1998 study [18] of peripheral neuropathy in HIV patients reported no statistical difference between real and sham acupuncture, further emphasizing uncertainties regarding its effectiveness in pain management. LINDE's 2005 research [27] on neurogenic headaches echoed these findings, showing no advantage of real acupuncture over superficial needling, which highlights the need for more investigation into how acupuncture interacts with the central nervous system in treating headaches. THOMAS' 2006 study [28] of non-specific low back pain showed no short-term difference between acupuncture and conventional treatments, although a significant difference was noted over the long term, raising critical questions about the duration and sustainability of acupuncture's benefits. Taken together, these studies highlight the need for further research to clarify acupuncture's role in treating various conditions, especially where subjective outcomes are involved. These findings suggest that in subjective conditions, where outcomes including pain relief are self-reported, non-specific factors such as patient expectations, placebo effects, or the therapeutic environment may play a larger

role in influencing results. The observation that minimally stimulated sham acupuncture frequently yields outcomes similar to those of genuine acupuncture challenges our understanding of the significance of acupoint specificity and needling depth. This pattern underscores that while acupuncture may be effective in conditions with objective physiological outcomes, its advantage in subjective conditions remains unclear, which is likely driven by broader psychological and environmental factors.

Acupuncture offers additional benefits to patients when integrated with conventional treatment. Several studies highlight the additional benefits of combining acupuncture with conventional treatment. For instance, CARDINI's 1998 study [17] on breech presentation enrolled 260 participants in a multicenter, randomized, controlled trial; the results demonstrated that moxibustion combined with standard acupuncture was superior to conventional treatment alone. Similarly, VICKERS' 2004 study [22] examined the impact of acupuncture on chronic headaches in 401 participants and found a significant difference between the group receiving traditional Chinese acupuncture in combination with conventional treatment and those receiving conventional treatment alone. Additionally, ELDEN's 2005 study [25], which involved 386 participants with pelvic pain, showed that acupuncture combined with conventional treatment, or conventional treatment plus exercise, significantly outperformed conventional treatment alone. These findings collectively demonstrate the promoted therapeutic benefits of integrating acupuncture with conventional medical treatments.

Overall, the "known knowns" from these RCTs in acupuncture highlight that while acupuncture can be effective for certain conditions, its efficacy is varied and often condition-specific. The mixed results across different studies highlight the importance of rigorous study design and the need for ongoing research to fully understand the potential and limitations of acupuncture in clinical practice.

2.2 Known unknowns (areas where knowledge is incomplete or uncertain)

The therapeutic efficacy of acupuncture, while widely practiced and supported by some clinical evidence, remains partly unknown in several areas. While there is a certain level of understanding of how acupuncture stimulates the nervous system, releases endorphins, and affects blood flow, the full range of its mechanisms remains unclear. How these effects translate into exact therapeutic benefits for specific conditions is not entirely mapped out. There are many claims about acupuncture's efficacy for various conditions, from chronic pain to mental health disorders, but conclusive evidence for some conditions is still lacking. Rigorous trials with consistent results are warranted to better understand which ailments acupuncture is truly effective for and which it isn't. Some individuals respond exceptionally well to acupuncture, while others experience no benefit. The reasons behind this difference in response — whether genetic, physiological, or psychological — are still unknown, leaving questions about who will benefit most from acupuncture. While short-term benefits, especially for pain relief, are often reported, the long-term therapeutic efficacy of acupuncture is less well understood. For some conditions, it remains unclear whether acupuncture provides sustained relief or if the effects diminish over time.

Despite the substantial number of RCTs conducted on acupuncture, several "known unknowns" persist, revealing gaps in our understanding and areas where further research is warranted. These unknowns pertain to the specific conditions treated, the mechanisms of action, and the comparative effectiveness of acupuncture techniques. These are the gaps in understanding that the trials reveal, where further research is needed.

(i) Mechanisms of acupuncture's efficacy. While it is established that acupuncture can activate neurobiological pathways, the exact mechanisms of how acupuncture leads to pain relief in some conditions while failing in others remain to be elucidated. This includes understanding why acupuncture works well for certain pathological conditions (e.g., nausea, urinary incontinence) but less effectively for pain-related issues in terms of comparing real acupuncture with sham acupuncture. Is the success tied to the specific neurochemical pathways activated, or are there other unknown factors influencing these outcomes?

(ii) Placebo vs. physiological effects. The ongoing debate between acupuncture's placebo effect and its true physiological benefits remains to be resolved. Trials conducted by CARDINI et al. [17] and SHEN et al. [19] show clear effectiveness, yet others [24, 27] fail to demonstrate superiority over sham acupuncture. The "known unknown" in these trials is whether the success of acupuncture is solely due to physiological effects, or if psychological factors, contextual influences, and patient expectations might play a more significant role than currently acknowledged.

(iii) Standard acupoints vs. random acupoints. In several trials, LEE et al. [5] and HINMAN et al. [33] show no difference between treatment at standard acupoints and random or superficial needling. This poses the question of whether the specificity of acupoints is clinically relevant. Further research is required to clarify the importance of precise acupoint targeting.

One area of uncertainty includes the treatment of chronic pain. LEE's 1975 study [5] of 261 patients found no significant difference between standard acupuncture points and arbitrary points, suggesting that the specific points used may not be crucial for pain relief. This provokes questions about the fundamental principles of

acupuncture point selection and whether factors such as the practitioner's technique or patient expectations play a larger part. Similarly, SHLAY's 1998 study [18] of neuropathic pain in acquired immune deficiency syndrome (AIDS) patients found no significant difference between true acupuncture and shallow, non-acupoint needling, echoing other findings in pain research. These results highlight the need for a better understanding of why acupuncture does not consistently outperform placebo treatments. Identifying the mechanisms by which acupuncture provides pain relief could refine techniques and potentiate its effectiveness.

Acupuncture's effectiveness in treating substance addiction is another area with considerable uncertainties. MARGOLIN's 2002 study [21] of cocaine addiction found no significant difference between standard ear acupuncture and relaxation training. This suggests that while acupuncture is being explored as a treatment for addiction, its efficacy in this area is not well-established. Understanding the underlying biological and psychological mechanisms by which acupuncture might influence addiction behaviors is crucial for developing more effective treatment protocols.

The use of acupuncture for reproductive health, especially in improving *in vitro* fertilization (IVF) outcomes, also presents uncertainties. SMITH's 2018 study [37] of IVF success rates found no significant difference between true acupuncture and non-insertive, non-acupoint stimulation. This poses questions about the potential physiological effects of acupuncture on reproductive processes and whether other factors, including timing and frequency of treatments, might influence outcomes.

In treating knee osteoarthritis, HINMAN's 2014 study [33] found no significant difference between true acupuncture and sham laser acupuncture. Similarly, LINDE's 2005 study [27] of neurogenic headaches also found no significant difference between true acupuncture and shallow, non-acupoint needling. These results, if their study designs are not being questioned, suggest that the therapeutic benefits of acupuncture for these conditions may be limited or influenced by placebo effects. Further research is needed to determine if specific subpopulations or different acupuncture protocols might yield more definitive benefits.

Acupuncture has shown promise in managing chemotherapy-induced nausea and vomiting, as demonstrated by SHEN's 2000 study [19] of 104 patients, which found that true acupuncture with low-frequency electrical stimulation was significantly more effective than sham acupuncture in reducing these symptoms. However, the precise mechanism by which acupuncture alleviates these effects remains unclear. Clarifying these mechanisms could help optimize acupuncture protocols for cancer patients, raising their quality of life during treatment. This area presents substantial potential for exploration and encourages a growing body of clinical research in major cancer centers across the United States [36, 39-41].

In the field of obstetrics, CARDINI's 1998 research [17] on breech presentation involving 260 patients found that moxibustion at standard acupuncture points was more effective than conventional treatment without moxibustion in correcting fetal position. This indicates a potential application for acupuncture and related techniques in obstetric care. In reproductive health, particularly in IVF outcomes, the evidence remains inconclusive. SMITH's 2018 study [37] on IVF success rates found no significant difference between true acupuncture and non-insertive, non-acupoint stimulation, indicating that acupuncture may not promote IVF outcomes.

The effectiveness of acupuncture in treating substance addiction, specifically cocaine addiction, appears to be less clear. MARGOLIN's 2002 study [21] involving 620 participants found no significant difference between standard ear acupuncture and relaxation training, suggesting that acupuncture may not be an effective standalone treatment for cocaine addiction, while BULLOCK's 1989 study [15] on alcohol addiction relapse found that electrical acupuncture at specific points was significantly more effective than at non-specific points.

For conditions such as knee osteoarthritis and tension-type headaches, the results are mixed. Study [27] of tension-type headaches both found no significant difference between true acupuncture and sham treatments. It needs to be replaced as HINMAN's 2014 study [33] of knee osteoarthritis and LINDE's 2005 study [27] of neurogenic headaches both found no significant difference between true acupuncture and sham treatments, which contradict the findings in other studies [22, 23, 26] of this review. However, some studies have shown positive results, such as LIU's 2017 research [34] on stress urinary incontinence, which found that true acupuncture with electroacupuncture was superior to sham electroacupuncture.

While RCTs have provided valuable insights into acupuncture's potential benefits, they have also highlighted significant "known unknowns" including uncertainties about the importance of specific acupuncture points, the mechanisms of action, and the conditions for which acupuncture is most effective. The dosage-effect relationship of acupuncture has been widely recognized and has garnered considerable attention recently, but efforts to quantify these relationships are insufficient. Addressing these unknowns through further rigorous research will be essential for integrating acupuncture more effectively into evidence-based medical practice.

2.3 Unknown knowns (overlooked or unconsciously accepted facts)

The "unknown knowns" from the clinical trials refer to insights or patterns that, despite being present, might be overlooked or dismissed. In reviewing the RCTs published in leading medical journals, a pattern emerges that

can be considered as an "unknown known" within the broader scientific discourse on acupuncture's effectiveness. These trials, which were meticulously designed and conducted across various conditions, consistently explored the efficacy of acupuncture against both sham treatments and conventional medical interventions. Despite the rigorous methodology, many of these studies reveal no statistical difference between real and sham acupuncture. This suggests that acupuncture's therapeutic efficacy may be attributable to placebo effects or psychological factors, rather than solely to the specific physiological mechanisms typically to it. Several potential "unknown knowns" in this context are explored as follows.

There are several facts about acupuncture that the medical community may have already been aware of but has yet to fully acknowledge or integrate into practice. One of these is the role of patient expectation in acupuncture's success. Many RCTs implicitly show that patient belief and expectation significantly contribute to acupuncture's therapeutic efficacy, particularly in subjective conditions like pain. However, this psychological component is often underestimated in the evaluation of acupuncture's efficacy. Another overlooked aspect is the variability in acupuncture's efficacy based on the specific condition. While it is well known that acupuncture is effective for specific conditions, such as nausea and incontinence, its inconsistent results across various conditions are not always considered a general treatment. This selective effectiveness implies that acupuncture should be applied in a more condition-specific manner than is currently the case. Furthermore, the reliance on acupoint specificity is another area where practice has not kept pace with the evidence. Numerous trials indicate that the exact location of needle insertion, whether at standard or random acupoints, may not affect outcomes markedly. Yet, the focus on acupoint precision remains a central element in the teaching and practice of acupuncture, despite evidence suggesting it may not be as critical as previously thought for certain conditions. For example, FUNG's 1986 study [12] of asthma, published in *The Lancet*, demonstrated a significant difference between real and sham acupuncture, implying potential benefits for respiratory conditions that may be overlooked. Besides, ABBATE's 1980 study [11] of pain management after thoracic surgery showed that electroacupuncture activated endorphins and decreased the need for additional painkillers, yet the importance of this method in post-surgery recovery remains underappreciated. JOBST's 1986 research [13] on disabling dyspnea demonstrated significant subjective improvements in patients, even in the absence of objective differences, which indicates that the role of patient expectations in acupuncture outcomes may be underemphasized. These findings suggest that certain aspects of acupuncture's effectiveness, while known, are not fully acknowledged in broader medical applications.

(i) Consistency in results across studies. Many studies show no significant difference between real acupuncture and sham acupuncture (e.g., for chronic pain, neuralgia, and osteoarthritis). This pattern indicates a potential placebo effect or the possibility that the specific placement of needles might not be as crucial as previously thought.

(ii) Effectiveness in specific conditions. While much research shows no significant difference between real and sham acupuncture, certain conditions, such as nausea and vomiting after chemotherapy and pain management in chest surgery, consistently show acupuncture's superior efficacy over control treatments. This indicates that acupuncture may be particularly effective in managing certain types of pain or physiological responses.

(iii) Influence of study design. Research with positive results for acupuncture often involves designs where the treatment is combined with other interventions, such as standard medical care. This implies that acupuncture may promote the effectiveness of conventional treatments for certain conditions.

(iv) Subtle differences in techniques. Some studies show that minor changes in technique or control group conditions (e.g., non-standard point placement) yielded significantly different results. This suggests that even subtle variations in acupuncture practice could affect outcomes, indicating that the practitioner's technique might play a more critical role than is currently acknowledged.

These findings with respect to "unknown knowns" suggest potential areas for further research or reevaluation of how acupuncture is used and explored. The "unknown knowns" — the recurring lack of significant difference between real and sham acupuncture — represent a critical insight that is both acknowledged and, at times, overlooked in discussions about acupuncture's clinical effectiveness. This challenges the traditional view that acupuncture's efficacy is primarily rooted in its classical principles, instead suggesting the substantial influence of patient expectations and the placebo effect. This pattern calls for a deeper reflection on how acupuncture is framed within medical practice and public perception, emphasizing the need for a more nuanced understanding of its role in patient care.

2.4 Unknown unknowns (unexpected findings or insights not previously considered)

RCTs in acupuncture have shed light on many aspects of its efficacy, yet they have also uncovered several "unknown unknowns" — areas where unexpected results and unexplored questions highlight the need for further investigation. These "unknown unknowns" are critical to advancing our comprehension of acupuncture and its potential applications.

Several unforeseen findings have emerged through acupuncture trials, challenging pre-study expectations. A

notable discovery is the absence of difference between real and sham acupuncture across various conditions. Some trials [21, 24, 27] demonstrated no statistical difference between real and sham acupuncture, even in large-scale controlled studies, challenging the assumption that real acupuncture consistently produces superior outcomes. Another unexpected insight is the efficacy of sham acupuncture. For instance, KAPTCHUK et al. [29] found that sham acupuncture outperformed placebo pills in managing conditions like arm pain, suggesting that sham acupuncture, which theoretically should not be effective, can still trigger significant therapeutic efficacy, potentially through psychological or non-specific pathways. Additionally, the discovery that transcutaneous electrical stimulation [7] can trigger endogenous opioid release was not widely anticipated. These findings reveal potential biological pathways that acupuncture may activate to reduce pain, adding complexity to the debate interplay between placebo and physiological effects.

Several additional trials have revealed surprising findings that were not anticipated. In WECHSLER's 2011 study [32] of asthma, no significant difference between drug inhalation and sham acupuncture was observed, which indicates unexpected complexities of how sham acupuncture interacts with chronic respiratory conditions. WU's 2017 research [35] on ovulation in polycystic ovary syndrome also found no statistical difference between real and sham acupuncture in stimulating ovulation, which is surprising given acupuncture's potential to regulate reproductive functions. Similarly, HINMAN's 2014 study [33] of knee osteoarthritis found no significant difference between real and sham acupuncture despite its large sample size, highlighting the need for further refinement in understanding acupuncture's role in treating osteoarthritis. These unexpected results suggest areas where the mechanisms of acupuncture require deeper exploration.

A thorough understanding of the placebo effect in acupuncture studies remains a substantial "unknown unknown". Understanding the extent and mechanisms of the placebo effect in acupuncture could provide valuable insights into the optimization of treatment protocols. Unexpected findings in studies such as KAPTCHUK's 2006 research [29] on arm pain, where sham acupuncture was more effective than a placebo pill, highlight the complexity of acupuncture's efficacy. These results suggest that even placebo or sham treatments can have varying degrees of efficacy, depending on how they are administered and perceived by patients. This variability introduces an "unknown unknown" in understanding the specific elements of acupuncture that contribute to its effectiveness.

The role of acupuncture in strengthening conventional treatments, as observed in VICKERS' 2004 study [22] of chronic headaches, where acupuncture combined with standard care was more effective than standard care alone, poses questions about the potential synergistic effects of acupuncture in combination with other therapies. This integration between alternative and conventional medicine represents a fertile ground for exploration, with "unknown unknowns" regarding the optimal integration of these approaches to maximize patient outcomes.

While RCTs have provided valuable insights into acupuncture, they have also uncovered numerous "unknown unknowns" that highlight the complexity and multifaceted nature of this traditional practice. These areas of uncertainty, including the precise mechanisms of action, the influence of patient-specific factors, the placebo effect, and the potential for synergy with conventional treatments, highlight the need for continued rigorous research to unravel its full potential and limitations.

3 Further discussion

The analysis of RCTs in acupuncture, published in four leading medical journals — JAMA, BMJ, *The Lancet*, and NEJM, provides a comprehensive overview of the high standards and impact these studies have in the medical community. Despite their small representation within the broader pool of acupuncture research, these RCTs are pivotal in shaping clinical guidelines, policy decisions, and further research due to their methodological rigor and the credibility of the journals in which they were published.

However, these RCTs also indicate significant challenges and variability in the field of acupuncture research. These research often manifests mixed results, with some demonstrating acupuncture's efficacy over placebo or standard treatments, while others indicating no significant differences. For example, acupuncture showed promising results in managing chemotherapy-induced nausea and vomiting, as noted in SHEN's 2000 study [19], and in correcting breech presentation in pregnancy, as highlighted by CARDINI's 1998 research [17]. Conversely, research on chronic pain, neuropathic pain in AIDS patients, and knee osteoarthritis, such as those by LEE et al. [5], SHLAY et al. [18], and HINMAN et al. [33], found no significant difference between true acupuncture and placebo treatments.

These mixed outcomes underscore the need for ongoing research to address the "known unknowns" and "unknown unknowns" in acupuncture studies. Key areas of uncertainty include the specific mechanisms through which acupuncture exerts its effects, the importance of acupuncture point selection, the potential placebo effect, and the variability in patient responses across different conditions. Additionally, the role of acupuncture as a complementary therapy, particularly its potential synergistic effects when combined with conventional treatments, presents a promising but underexplored area for research.

The challenges arising from the various types of knowledge — "known knowns, known unknowns, unknown knowns, and unknown unknowns" — within the context of acupuncture clinical trials can be effectively addressed through systematic reviews and meta-analyses. These methodologies have become increasingly prominent in acupuncture research, which offer a structured approach to synthesizing data and drawing more reliable conclusions. However, even with these advanced analytical techniques, the moderate significance of results often seen in such studies continues to present a challenge. This limitation compromises the effect size, highlighting the ongoing issue that underscores the complexity of evaluating acupuncture's efficacy through traditional research frameworks [42-47].

While RCTs in acupuncture published in prestigious journals highlight the therapy's potential and contribute to its increasing usage in the medical community, it also exposes the complexities and uncertainties that continue to challenge its integration into mainstream medical practice. Addressing these challenges through further rigorous research is essential to fully understanding and optimizing its therapeutic potential.

The inherent challenge in designing a control group for acupuncture trials lies in the physiological responses triggered by any form of skin penetration, regardless of whether the needles are placed at classical acupuncture points or non-acupoints. This issue is evident in many of the RCTs published in top medical journals, where the chosen control groups, such as superficial needling at non-acupoints or even no stimulation, may still elicit biological and physiological responses. These responses can include the activation of nerve endings, the release of endorphins, and changes in local blood flow, all of which may contribute to therapeutic efficacy independent of the specific acupoint targeted [48]. Consequently, the observed reduction in differences between treatment groups and control groups in these studies could be attributable to the control interventions not being inert. This sparked fierce debates among acupuncture researchers.

In examining the 34 RCTs published in JAMA, BMJ, *The Lancet*, and NEJM, it becomes apparent that many control designs fall into the above category, thereby complicating the interpretation of results. When sham acupuncture or superficial needling is employed as a control, it may not serve as a true placebo but rather as a less potent version of the intervention. This may blur the distinction between the actual therapeutic efficacy of acupuncture and those elicited merely by the act of needling itself. As a result, the frequent observation of "no significant difference" between real and sham acupuncture across various studies may be misleading. Instead of demonstrating acupuncture's lack of efficacy, these findings might be a reflection of the inadequacy of the control methods in isolating the specific effects of acupuncture. For future studies, more refined and innovative control strategies are needed to provide clearer insights into acupuncture's true clinical value, which remains obscured by the limitations of current sham controls.

The non-inert nature of the control designs used in nearly all acupuncture RCTs [49] has led to a relatively modest proportion of positive results in English-language literature, which stands at just 62.03%. Among these studies, a significant portion (44.3%) were authored by Chinese researchers, who reported a higher positive result rate at 71.43%. In contrast, the positive result rate in studies authored by non-Chinese scholars was notably lower, at only 59.18% [50]. This disparity suggests that if a truly inert sham control were used in these trials, the positive result rate might be significantly higher, reflecting a more accurate measure of acupuncture's efficacy.

However, thousands of RCTs in acupuncture have already been published in non-Chinese-language medical journals over the past 50 years, ranging from nursing journals to top-tier medical journals. Given this extensive body of literature, the question arises as to whether there is still an opportunity to correct the current understanding and perceptions of acupuncture through further RCTs. The vast number of existing studies suggests that simply increasing the quantity of RCTs may not be sufficient. Instead, there may be a need for a paradigm shift in the design and methodology of these studies to address the inherent issues with control groups and to provide a clearer, more accurate picture of acupuncture's true therapeutic potential. Only with such methodological improvements can the scientific community hope to resolve the ongoing debates and misconceptions about acupuncture [51-55].

Moreover, if treatments based on classical acupuncture theory consistently yield results that are no better than those produced by inert sham procedures in numerous rigorous clinical trials, it poses an important question: should we reconsider and potentially reassess the foundational principles of classical acupuncture theory? This recurring pattern of indistinguishable outcomes suggests that our traditional understanding may need to be re-evaluated in light of contemporary scientific evidence [56-59].

Among this sample of RCTs, conclusive interpretations are difficult due to contradictory outcomes observed across different studies examining the same or similar conditions, such as asthma [12, 32], knee osteoarthritis [23, 26, 30, 33], and addiction [15, 21]. These inconsistencies highlight the challenges in drawing definitive conclusions about acupuncture's efficacy for these conditions, which emphasize the need for more standardized methodologies and outcome measures to enable better comparison and replication of results.

Although this is a macro study on RCTs, it highlights the pressing need for more standardized methods in acupuncture research, particularly in acupoint selection, needle technique, and outcome assessment for the same condition. The absence of consistency in these areas often undermines the reliability and comparability of research findings. Studies commonly adopt varying acupoints, needling depths, stimulation techniques, and outcome measures, making it difficult to draw definitive conclusions establishing standardized protocols for these parameters is essential to ensure consistency and replicability. Future acupuncture trials must prioritize consistency in these aspects to increase the credibility of the research and facilitate more robust data aggregation through systematic reviews and meta-analyses.

Additionally, the adoption of the Revised Standards for Reporting Interventions in Clinical Trials of Acupuncture (STRICTA), an extension of the Consolidated Standards of Reporting Trials (CONSORT) statement, marks a considerable advancement in the standardization of acupuncture research. STRICTA guidelines ensure that key details about acupuncture interventions, including the rationale for point selection, needling techniques, and treatment regimens, are reported consistently. This transparency promotes better replication of studies and strengthens the overall trustworthiness of acupuncture research. Adherence to these guidelines in future studies will not only bolster the evidence base but also yield meaningful comparisons across trials.

From a clinical perspective, the inclusion of acupuncture in disease guidelines — thanks to high-quality trials — signals the growing acceptance of its therapeutic potential. However, further research is needed to investigate how acupuncture can be optimally integrated with conventional treatments. Developing personalized treatment plans that account for individuals' characteristics, such as medical history, constitution, and previous treatment responses, could promote the effectiveness of acupuncture. Rigorous investigation into these personalized approaches will be key to establishing protocols that can be integrated into broader clinical practice guidelines.

Finally, traditional acupuncture theory must evolve in response to modern scientific findings to remain effective in guiding clinical practice. While acupuncture's roots lie in concepts such as Qi and meridians, modern research into neural pathways and physiological responses provides valuable insights into its mechanisms. Reflecting on and integrating these scientific findings will ensure that acupuncture not only retains its essence but also adapts to the needs of modern healthcare. This evolution will strengthen the integration of acupuncture with contemporary medical practices, ultimately benefiting both patients and practitioners.

4 Conclusion

The growing number of RCTs in acupuncture, now surpassing 14 000, signifies a robust and expanding field of research. By examining a selected sample of studies published in top medical journals, we gain valuable insights into the quality, challenges, and advancements within acupuncture research. These high-quality RCTs not only validate the clinical relevance of acupuncture but also highlight the critical issues that must be addressed to further advance the field. Through ongoing rigorous research and methodological improvements, the potential of acupuncture as a scientifically validated therapeutic modality can be fully realized, ultimately benefiting patients and healthcare systems worldwide.

The exploration of acupuncture through the lens of the Rumsfeld Matrix on the RCTs shows a complex and multifaceted landscape of knowledge. While the integration of RCTs has brought a new level of academic rigor to acupuncture research, it has also highlighted the challenges inherent in evaluating a treatment modality rooted in traditional practices and holistic approaches. The studies published in top medical journals such as JAMA, BMJ, *The Lancet*, and NEJM underscore both the potential and the limitations of acupuncture, implying "known knowns" about its effectiveness in certain conditions, while also uncovering "known unknowns" and "unknown unknowns" that continue to question our understanding.

One of the most important findings from this investigation is the recurring issue with control group designs in RCTs in acupuncture. The physiological responses triggered by any form of needling, regardless of the acupoint used, complicate the interpretation of results and may obscure the true efficacy. This issue is particularly evident in the common observation of no significant difference between real and sham acupuncture, which may reflect the inadequacy of current control methods rather than a lack of therapeutic efficacy.

The 34 RCTs published in top medical journals offer a comprehensive view of acupuncture research, indicating both well-established findings and areas of uncertainty. The "known knowns" confirm acupuncture's efficacy in specific conditions, such as nausea and urinary incontinence, and consistently demonstrate brain responses. However, the "known unknowns" expose gaps in understanding the mechanisms behind acupuncture's efficacy and its varying efficacy across conditions, especially in pain relief. Additionally, the "unknown knowns" point to overlooked factors such as patient expectations and the questionable emphasis on acupoint specificity, while the "unknown unknowns" demonstrate surprising outcomes. This analysis underscores the need for a more nuanced approach to acupuncture research, recognizing its established benefits while exploring unresolved issues to guide future studies and clinical applications.

The Rumsfeld Matrix examination identified in this study, such as the potential placebo effect and the variability in patient responses, warrants a more nuanced approach to acupuncture research. Future studies must refine control strategies to better isolate the specific effects of acupuncture and explore the underlying mechanisms that contribute to its therapeutic potential. As acupuncture continues to gain acceptance in the medical community, addressing these challenges through rigorous and innovative research is key to fully integrating this traditional practice into evidence-based medicine. The ongoing evolution of acupuncture research promises to deepen our understanding of this ancient therapy, offering new insights into and opportunities for improving patient care.

A limitation of this study lies in the generalizability of its findings. The trials selected from the top four leading journals may not fully represent the diversity of acupuncture practices worldwide, as study designs, patient demographics, practitioner expertise, and acupuncture techniques can vary considerably across regions and populations. This variability restricts the broader applicability of the conclusions drawn in the paper.

Competing interests

The authors declare no conflict of interest.

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罗姆斯菲尔德矩阵在针灸临床试验中的应用

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【摘要】本研究考察了罗姆斯菲尔德矩阵在针灸临床试验中的应用，重点关注发表在《美国医学会杂志》《英国医学杂志》《柳叶刀》和《新英格兰医学杂志》等顶级医学期刊上的临床试验研究（RCTs）。随机临床试验的整合一定程度上强化了针灸研究的学术严谨性，挑战了传统的决定论模型，并揭示了一个复杂的领域：已知的已知、已知的未知、未知的已知和未知的未知。虽然 RCTs 验证了针灸在某些病症中的疗效，但也突显了相当大的挑战，包括对照组设计的局限性和安慰剂效应的潜在影响。许多研究中真实针灸和假针灸之间无显著差异问题的反复出现强调了需要更完善的对照策略和对针灸机制更细致的理解。此项研究呼吁继续开展严谨的针灸研究，以充分探索针灸的治疗潜力及与循证医学的融合，最终有助于改善患者护理并在医学界获得更广泛的接受度。

【关键词】针灸；随机临床试验；罗姆斯菲尔德矩阵；安慰剂效应；对照组设计；治疗潜力