REVIEW
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# Annual advances of acupuncture research in 2022

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***Author contributions***

Kai Zhang and Mei-Dan Zhao contributed to the conception and design of the work. Jia-Qi Li and Wen-jing Huang drafted the manuscript. Kai Zhang and Mei-Dan Zhao revised the manuscript. All authors have read and approved the manuscript.

***Competing interests***

The authors declare no conflicts of interest.

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***Peer review information***

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***Abbreviations***

COVID-19, new coronary pneumonia; CRF, cancer-related fatigue; DMARDs, disease-modifying anti-rheumatic drugs.

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***Abstract***

This article reviews the major advances in acupuncture research in 2022, including clinical reports, basic research, and reviews. In terms of the type of literature, most of them are systematic reviews and clinical trials, while high-quality basic studies can also be found. The innovative inventions and researches in this field are of increasing quality and in a wide range of fields, acupuncture is attracting more and more attention in the international arena. In particular, some acupuncture combined sensors such as $H_2$ -EC/SD co-therapy, precise positioning, and vivo monitoring of neurotransmitter has been used for oncological diseases and neuropathic pain. Acupuncture has been shown to be beneficial in the treatment of pain, stroke, psychiatric disorders, cancer, COVID-19 and others. Most of the studies show that acupuncture can play a positive role in various diseases and provide evidence for clinical applications and mechanism research.

**Keywords:** acupuncture; pain; stroke; cancer; COVID-19; review

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***Highlights***

1. An overview of the acupuncture literature as of 2022 is given in this review. The content focused on clinical research, including pain, stroke, psychosomatic disorders, cancer, COVID-19, and others, as well as basic research and reviews.
2. International guidelines on tumor-related pain have been introduced. In basic research, acupuncture sensors have been crucial for the detection and treatment of tumors and osteoarthritis, as well as in the detection of neurotransmitters. In clinical trials, the efficiency of acupuncture in treating a variety of diseases has been further supported by the findings of numerous high-quality randomized controlled studies.

***Background***

Acupuncture is a type of non-pharmacologic treatment with few side effects, that is performed by stimulating acupoints with instruments like acupuncture or electroacupuncture needles to treat or prevent various diseases. According to a report from the World Federation of Acupuncture-Moxibustion Societies, acupuncture has been utilized all over the world [1]. In recent years, acupuncture-related basic and clinical research has made good progress, and an increasing number of high-quality studies have been conducted [2–4]. In order to build a comprehensive understanding of the progress of acupuncture for disease management, we summarized studies published in 2022 via PubMed, and in all, 3,456 articles were identified. Of these, there were 535 reviews, 217 meta-analyses, 337 clinical studies, 564 animal-based studies, and others. The number of published articles has shown a significant growth trend in the past decade, with the 2022 figure nearly doubling that of 2012 (Figure 1). The most common acupuncture-related studies in diseases in 2022 were: pain, stroke, depression, cancer, and new coronary pneumonia (COVID-19) (Table 1). In addition, the application of some sensing needles has been reported. The keywords of acupuncture research in these 10 years and 2022 were shown in Figure 2 and Figure 3 based on CiteSpace [5], respectively. Based on the frequency and centrality of the visualization analysis, we found that the popular keywords in 2022 were “systematic review”, “randomized controlled trial”, “traditional Chinese medicine”, “acupuncture and moxibustion”, and “complementary medicine” which had a high frequency and centrality. The network map of affiliations is shown in Figure 4, it shows that the affiliations with the largest number of published acupuncture research were the National Clinical Research Center for Chinese Medicine Acupuncture (79), First Teaching Hospital of Tianjin University of Traditional Chinese Medicine (64), Tianjin University of Traditional Chinese Medicine (32), and Hospital of Chengdu University of Traditional Chinese Medicine (30). The top five authors who published articles on acupuncture in 2022 were Wang Yu (39), Liang Fangrong (26), Li Jing (23), Liu Cunzhi (23) and Lee Myeong Soo (21) in Figure 5. The journals of high co-citation were *PLoS One* (230), *Evid-Based Compl Alt* (216), *Sci Rep-UK* (162), *Int J Mol Sci* (137), and *Lancet* (133). The most cited articles were conducted by Raman B et al. [6] (46), de Sire A et al. [7] (30), Becker CM et al. [8] (29), Stefanou MI et al. [9] (23) and Weintraub D et al. [10] (17) in Table 2 and Table 3.

***Pain-related conditions***

Guidelines and consensus statements have been published on acupuncture for treating pain conditions. The Association of Chinese and Western Medical Oncology has issued guidelines for *Integrative*

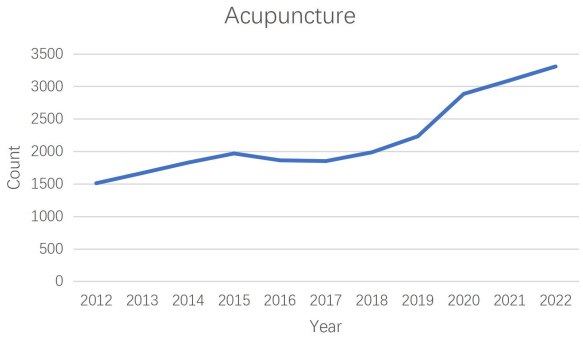



**Figure 1 Number of published articles from 2012 to 2022**

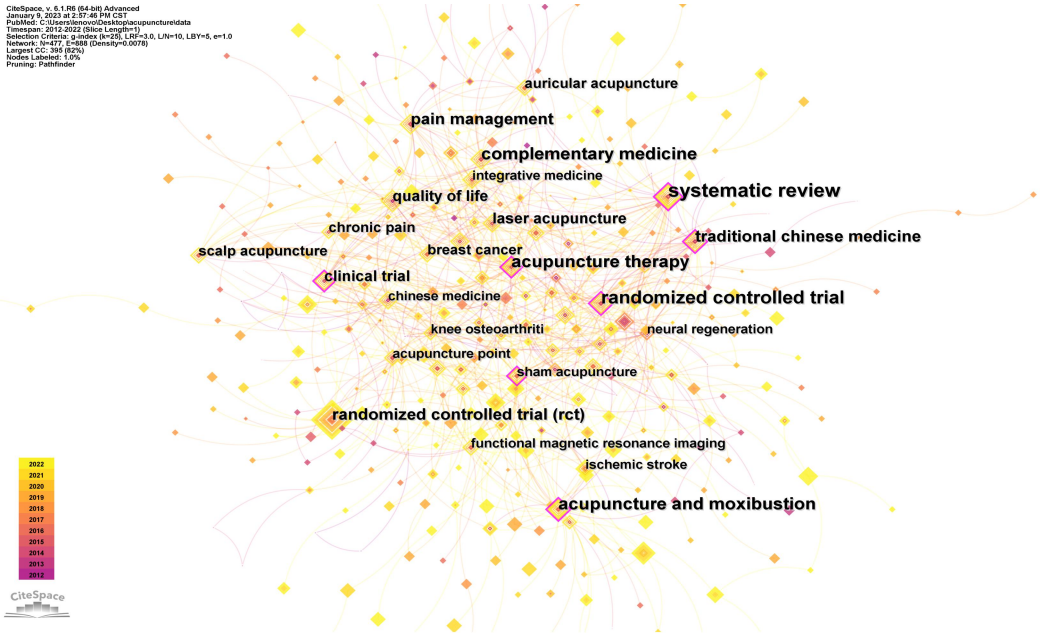



**Figure 2 Network map of keywords on acupuncture from 2012 to 2022**

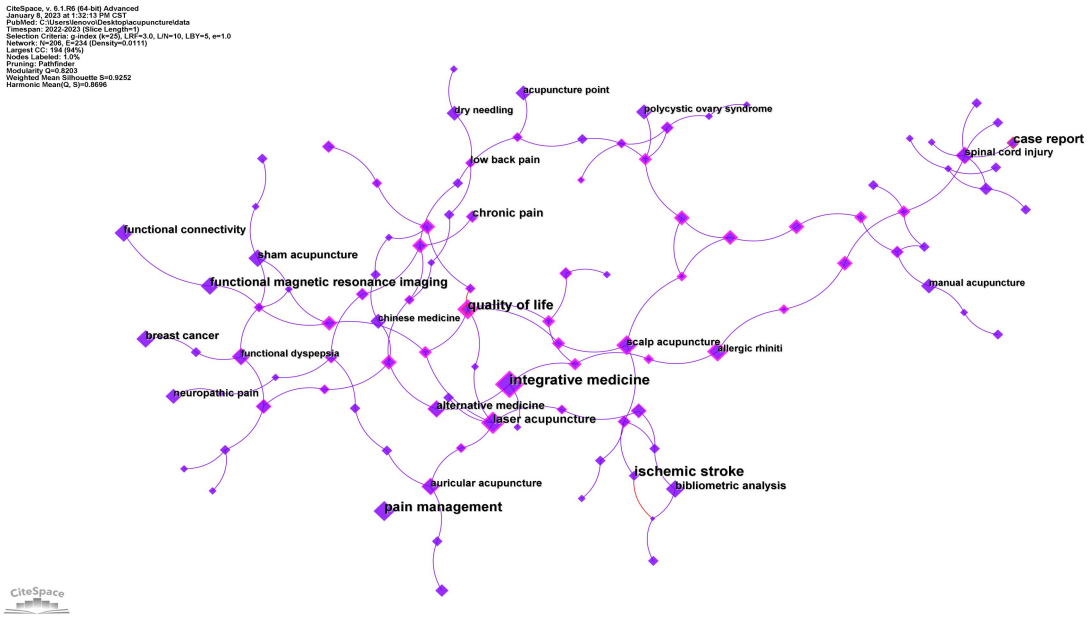



**Figure 3 Network map of keywords on acupuncture in 2022**

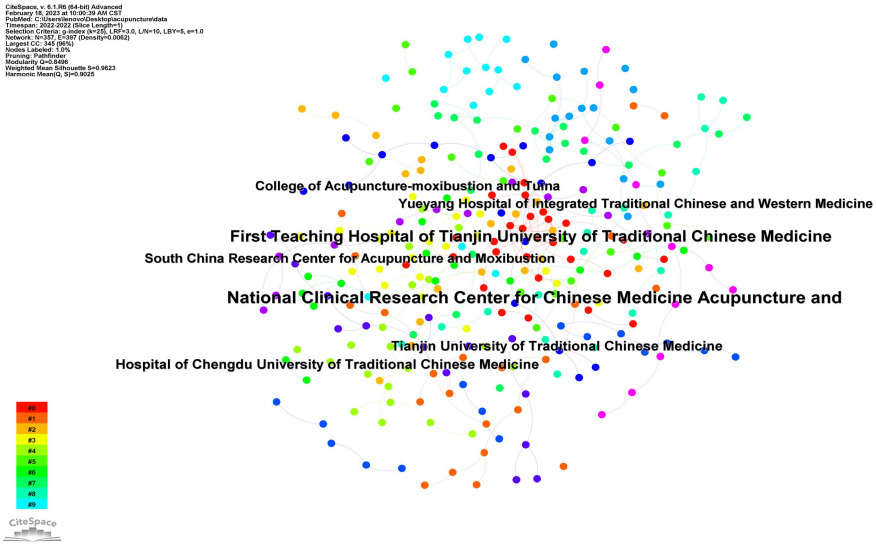



**Figure 4 Network map of affiliations with the most published articles on acupuncture in 2022**

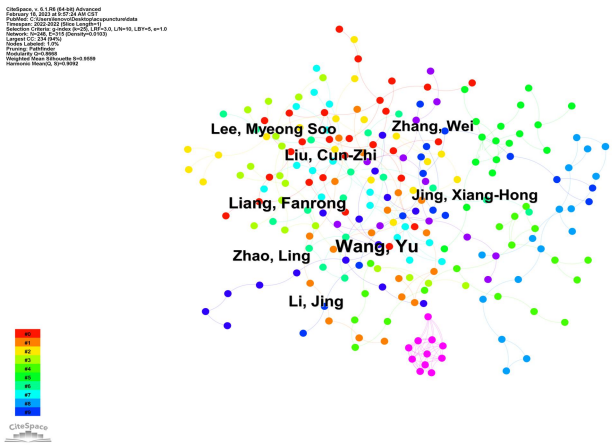



**Figure 5 Network map of authors with the most published articles on acupuncture in 2022**

**Table 1 Evidence of acupuncture treatment of diseases in 2022**

| | Disease (model) | Study design | Main outcomes | Effect |
|---|---|---|---|---|
| Pain | Musculoskeletal pain [11] | Meta-analysis | Significantly altered cerebral regions (defined by MNI/Talairach coordinates, cluster size, and statistical threshold), clinical assessment outcomes, correlations between imaging | Positive |
| | Post-stroke shoulder pain [12] | Meta-analysis | Shoulder pain, upper limb motor function, ADL, ROM | Positive |
| | Inflammatory pain [13] | Animal experiments | PWMT, mechanical allodynia, WB, qPCR, immunofluorescence detection (GRK2, Iba1, iNOS, TNF-α, IL-1β, CD206, IL-4, IL-10, GF-β) | Positive |
| | Pain (visceral-somatic pain) [14] | Animal experiments | Number of abdominal writhing response time to formalin | Positive |
| | Trigeminal neuralgia [15] | Animal experiments | Golgi-Cox staining (synaptic plasticity) | Positive |
| | Acute renal colic due to urolithiasis [16] | RCT | VAS score | Positive |
| | Cesarean delivery [17] | RCT | VRS, adverse effects, analgesics consumption, time to mobilization and Foley catheter removal, quality of patient blinding to randomization, satisfaction with treatment of pain | Positive |
| | Chronic tension-type headache [18] | RCT | Responder rate | Positive |
| | Tension-type headaches [19] | RCT | Responder rate | Positive |
| | Aromatase inhibitor-related joint pain [20] | RCT | BPI-WP | Positive |
| Stroke | Spastic hypertension after ischemic stroke [21] | Animal experiments | Laser speckle imaging, functional assessments (NFS, muscular tension scale, foot balance test, and gait analysis), H-reflex recording, TTC, WB, RT-qPCR, ELISA, IFA (GABA, KCC2, GABAAγ2) | Positive |
| | Stroke (MCAO/R) [22] | Animal experiments | 16S rRNA gene sequencing, liquid chromatography-mass spectrometry metabolomics species diversity, abundance of pathogenic bacteria, neurological issues, cerebral infarct dimensions, IL-6, IL-1β, TNF-α, SOD, MDA, BDNF | Positive |
| | Ischemic stroke (MCAO/R) [23] | Animal experiments | ladder rung walking test, ICA | Positive |
| | Post-stroke dysphagia [24] | Propensity score-matched cohort study | incidence of dysphagia | Positive |
| | Stroke [25] | Retrospective Cohort Study | NIHSS, BI scores | Positive (plus TCHM) |
| Depression | Major depressive disorder [26] | Meta-analysis | HAMD | Positive |
| | Postpartum depression [27] | Meta-analysis | HAMD, EPDS, effective rate, and estradiol levels. | Positive |
| | Ameliorating concomitant or residual insomnia with depression [28] | Meta-analysis | PSQI, HAMD | Positive |
| | Depression (CMS) [29] | Animal experiments | SPT, FST, NF-κB, p-NF-κB, inhibitor of NF-κB, p-IκBα, NOD-like receptor protein 3, IL-6, IL-1β, IL-18, TNF-α | Positive |
| | Depression (CRS) [30] | Animal experiments | body weight, SPT, immunofluorescence, WB, ELISA (microglial activation, HMGB1, IL-10, TNF-α) | Positive |
| | Insomnia and depression [31] | RCT | PSQI, HAMD, SAS | Positive |

**Table 1 Evidence of acupuncture treatment of diseases in 2022 (*continued*)**

| | Disease (model) | Study design | Main outcomes | Effect |
|---|---|---|---|---|
| Cancer | Cancer-related insomnia [32] | Meta-analysis | PSQI | Positive |
| | Sleep disturbances in cancer survivors [33] | Meta-analysis | PSQI, ISI | Ineffective |
| | Cancer-related fatigue [34] | Meta-analysis | The clinical efficiency (total effective rate or cure rate; clinical symptom integral), QOL | Positive |
| | Lung cancer [35] | Meta-analysis | sKPS, EORTC, , FACT, LCQ, MOS, SF-36, SGRQ | Positive |
| | Chemotherapy-induced peripheral neuropathy [36] | RCT | FACT-Tax, EORTC | Positive |
| | Cancer-related fatigue (CRF) [37] | Animal experiments | FST, OFT, WB ELISA, 16S rRNA sequencing, serum metabolomic analysis (gut microbiota, ZO-1, occludin, claudin-5, CRH, CORT, ACTH) | Positive |
| | Progressive gastric cancer [38] | RCT | Intraabdominal pressure, bowel sounds, physical function, role function, emotional function, cognitive function, social function | Positive |
| | Chemotherapy-induced nausea and vomiting [39] | retrospective study | Frequency of nausea and vomiting, ECOG-PS score, the adverse events | Positive |
| | Cancer-related conditions [40] | Systematic review | Expression of conclusion | Positive |
| COVID-19 | COVID-19 [41] | RCT | SpO2, RR | Positive |
| Others | Overactive bladder [42] | Meta-analysis | Number of participants whose OAB symptoms were cured or improved<br>Number of major adverse events<br>Number of minor adverse events | Positive uncertainly |
| | Rheumatoid arthritis [43] | Meta-analysis | DAS28, VAS, morning stiffness time, CRP, ESR, RF, AEs | Positive |
| | Respiratory diseases [44] | Meta-analysis | Inflammatory cytokines, lung function test | Positive |
| | Osteoarthritis [45] | Animal experiments | Morphological staining immunofluorescence detection (OARSI scores, MSCs, collagen II, MMP-13) | Positive |
| | Surgical pain-induced delirium-like behavior [46] | Animal experiments | PWMT, Hargreaves test, OFT, Y maze test, buried food test, Iba1 staining, immunohistochemistry (gut microbiota, microglia activation, and dynamic changes) | Positive |
| | Intervertebral disc degeneration [47] | Animal experiments | Cell viability assay, ROS level, SA-β-Gal staining, RT-qPCR (p16INK4a, CB2R, SA-β-gal, SASP, HMGB1, Col-2, SOX9, Col-X) | Positive |
| | Irritable bowel syndrome [48] | RCT | Responder rate | Positive |
| | Anxiety with Parkinson disease [49] | RCT | HAM-A, UPDRS, PDQ-39, ACTH, CORT | Positive |

MNI, Montreal Neuroimaging Institute; ADL, activities of daily living; ROM, range of motion; RCT, randomized controlled trial; PWMT, mechanical paw withdrawal threshold; WB, Western blot; qPCR, quantitative polymerase chain reaction; GRK2, G protein coupled receptor kinase 2; Iba1, ionized calcium binding adapter molecule 1; iNOS, inducible nitric oxide synthase; TNF, tumor necrosis factor; IL, interleukin; GF, growth factor; VAS, visual analog scale; BPI-WP, brief pain inventory worst pain; VRS, Verbal Rating Scale; NFS, Neurologic Function Scale; TTC, triphenyte-trazoliumchloride; ELISA, enzyme linked immunosorbent assay; IFA, immunofluorescence molecular assay; GABA, Γ-aminobutyric acid; KCC, recombinant potassium chloride cotransporters; MCAO/R, middle cerebral artery occlusion/reperfusion; ICA, independent component analysis; MS, mass spectrometry; SOD, superoxide dismutase; MDA, malondialdehyde; BDNF, brain-derived neurotrophic factor; ICA, independent component analysis; NIHS, National Institute of Health Stroke Scale; BI, Barthel Index; TCHM, traditional chinese herbal medicine; HAMD, Hamilton Rating Scale For Depression; EPDS, Edinburgh Postnatal Depression Scale; PSQI, Pittsburgh Sleep Quality Index; CMS, chronic mild stress; SPT, sucrose preference test; FST, forced swimming test; NF-κB, nuclear factor-kappa B; CRS, chronic restraint stress; SPT, sucrose preference test; SAS, Self-Rating Anxiety Scale; ISI, Insomnia Severity Index; FACT, functional assessment of cancer therapy; QOL, quality of life; sKPS, Karnofsky performance status; EORTC, European Organization For Research And Treatment of Cancer Quality of Life Questionnaire; LCQ, Leicester Cough Questionnaire; MOS, medical outcomes study; SF-36, item short form health survey; SGRQ, St George's Respiratory Questionnaire; OFT, open field test; ZO, zonula occludens; CRH, corticotropin releasing hormone; ACTH, adrenocorticotropic hormone; CORT, cortisol; ECOG-PS, Eastern Cooperative Oncology Group performance status; SpO2, oxygen saturation; RR, respiratory rate; OAB, overactive bladder; DAS28, Disease Activity Score of 28 joints; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; RF, rheumatoid factor; AEs, the occurrence of adverse reactions; MSC, mesenchymal stem cell; MMP, matrix metalloproteinase; RT-qPCR, reverse transcription quantitative polymerase chain reaction; CB2R, cannabinoid type 2 receptor; SASP, senescence-related secretory phenotypes; HMGB1, high mobility group protein; Col-2, collagen type II; SOX9, sry-box transcription factor 9; Col-X, collagen type X; HAMA, Hamilton Anxiety Scale; UPDRS, Unified Parkinson Disease Rating Scale; PDQ, Parkinson Disease Questionnaire.

**Table 2 The most cited articles on web of science on acupuncture in 2022**

| Rank | Authors | Title | Journal | Citation | DOI |
|---|---|---|---|---|---|
| 1 | Iyaswamy A | Theranostic F-SLOH mitigates Alzheimer's disease pathology involving TFEB and ameliorates cognitive functions in Alzheimer's disease models | *Redox Biol* | 23 | 10.1016/j.redox.2022.102280 |
| 2 | Lu LM | Evidence on acupuncture therapies is underused in clinical practice and health policy | *BMJ-Brit Med J* | 19 | 10.1136/bmj-2021-067475 |
| 3 | Ferrillo M | Efficacy of rehabilitation on reducing pain in muscle-related temporomandibular disorders: a systematic review and meta-analysis of randomized controlled trials | *J Back Musculoskelet* | 19 | 10.3233/BMR-210236 |
| 4 | Xu CH | A highly selective and sensitive biosensor for dopamine based on a surface molecularly imprinted layer to coordinate nano-interface functionalized acupuncture needle | *Chem Eng J* | 17 | 10.1016/j.cej.2022.135203 |
| 5 | Sreenivasmurthy SG | Protopine promotes the proteasomal degradation of pathological tau in Alzheimer's disease models via HDAC6 inhibition | *Phytomedicine* | 17 | 10.1016/j.phymed.2021.153887 |
| 6 | Onose G | Cellular and molecular targets for non-invasive, non-pharmacological therapeutic/rehabilitative interventions in acute ischemic stroke | *Int J Mol Sci* | 17 | 10.3390/ijms23020907 |
| 7 | Chen C | Tannic acid: a crosslinker leading to versatile functional polymeric networks: a review | *RSC Adv* | 16 | 10.1039/d1ra07657d |
| 8 | Wu CJ | Exploiting the twisted intramolecular charge transfer effect to construct a wash-free solvatochromic fluorescent lipid droplet probe for fatty liver disease diagnosis | *Anal Chem* | 15 | 10.1021/acs.analchem.1c04847 |
| 9 | D'Alessandro EG | Acupuncture for chemotherapy-induced peripheral neuropathy: a randomised controlled pilot study | *BMJ Support Palliat* | 15 | 10.1136/bmjspcare-2018-001542 |
| 10 | Jiang XK | EIF4A3-induced circARHGAP29 promotes aerobic glycolysis in docetaxel-resistant prostate cancer through IGF2BP2/c-Myc/LDHA signaling | *Cancer Res* | 15 | 10.1158/0008-5472.CAN-21-2988 |

**Table 3 The most cited articles on acupuncture in 2022**

| Rank | Authors | Title | Journal | Citation | DOI |
|---|---|---|---|---|---|
| 1 | Raman B | Long COVID: post-acute sequelae of COVID-19 with a cardiovascular focus | *Eur Heart J* | 46 | 10.1093/eurheartj/ehac031 |
| 2 | de Sire A | Sarcopenic dysphagia, malnutrition, and oral frailty in elderly: a comprehensive review | *Nutrients* | 30 | 10.3390/nu14050982 |
| 3 | Becker CM | ESHRE guideline: endometriosis | *Hum Reprod Open* | 29 | 10.1093/hropen/hoac009 |
| 4 | Stefanou MI | Neurological manifestations of long-COVID syndrome: a narrative review | *Ther Adv Chronic Dis* | 23 | 110.1177/20406223221076890 |
| 5 | Weintraub D | The neuropsychiatry of Parkinson's disease: advances and challenges | *Lancet Neurol* | 17 | 10.1016/s1474-4422(21)00330-6 |
| 6 | Kazeminasab S | Neck pain: global epidemiology, trends and risk factors | *BMC Musculoskelet Disord* | 16 | 10.1186/s12891-021-04957-4 |
| 7 | Yelin D | ESCMID rapid guidelines for assessment and management of long COVID | *Clin Microbiol Infect* | 15 | 10.1016/j.cmi.2022.02.018 |
| 8 | Chen ZR | Role of cholinergic signaling in Alzheimer's disease | *Molecules* | 14 | 10.3390/molecules27061816 |
| 9 | Iyaswamy A | Theranostic F-SLOH mitigates Alzheimer's disease pathology involving TFEB and ameliorates cognitive functions in Alzheimer's disease models | *Redox Biol* | 13 | 10.1016/j.redox.2022.102280 |
| 10 | Lu L | Evidence on acupuncture therapies is underused in clinical practice and health policy | *BMJ* | 13 | 10.1136/bmj-2021-067475 |

*Medicine for Pain Management in Oncology*. Acupuncture should be suggested for joint aches brought on by aromatase inhibitors in adult patients. Reflexology, acupressure, or acupuncture may be recommended for musculoskeletal pain or general cancer discomfort [50]. The *Academic Consortium Pain Working Group White Paper* has been updated, and it was reported that acupuncture can serve as an effective nonpharmacologic therapy for integrated acute pain management [51].

In basic research, neuronal G protein-coupled receptor kinase 2 modulates microglial activation, which may be a possible target for electroacupuncture analgesia and pain management, and contributes to electroacupuncture analgesia in mice for inflammatory pain [13]. Injury-inhibiting effects of manual acupuncture in the vagal ear branch and their lateral dependence on the left auricular branch of the vagus nerve stimulation in a visceral and somatic acute pain model [14]. In a animal model of trigeminal neuralgia, electroacupuncture reduces aberrant orofacial pain and anxiety-like behaviors by modifying synaptic plasticity in the CA1 hippocampal area [15]. It was found that acupuncture suppressed the neuronal activity triggered by neuropathic pain by decreasing the pain-related ion channel activation and inhibiting the release of inflammatory cytokines and chemokines from glial cells. Acupuncture also activates the pain control system by increasing levels of 5-hydroxytryptamine, norepinephrine, and opioid peptides in the spinal cord or brain [51]. Structures like the thalamus, insula, caudate, claustrum and lentiform nucleus all have clusters of activation in response to acupuncture, which provides some insight into the potential mechanisms by which acupuncture can modulate the above different brain regions for the treatment of musculoskeletal pain with acupuncture [11]. Acupuncture combined with rehabilitation training has been shown to be more efficient than rehabilitation training individually in improving shoulder pain, range of motion, upper extremity motor function, and activities of daily living in patients with poststroke shoulder pain [12].

In clinical trials, one study found that acupuncture may be considered an optional supplemental therapy in treating acute renal colic since it is benign and offers rapid and significant pain relief for individuals with renal colic compared to sham acupuncture in an emergency. Another study showed that acupuncture proved a safe and efficient way to lessen discomfort and hasten patient movement after cesarean delivery. Acupuncture may be recommended as a regular, additional therapy for pain management in individuals who have undergone elective cesarean delivery while keeping personnel and time costs in mind [17]. According to research, acupuncture may be beneficial in treating chronic tension-type headaches, since it has been demonstrated to reduce headache days for many chronic tension-type headaches sufferers by half or more and to continue for months even after acupuncture sessions are discontinued. The 8-week acupuncture treatment was effective in preventing chronic tension-type headaches, which provided a choice to control the cost-effectiveness of acupuncture therapy [18, 19]. Women who received 12 weeks of true acupuncture in a randomized clinical study for joint pain spurred on by aromatase inhibitors had less pain after 52 weeks compared to controls, indicating the long-term efficacy of this treatment [2].

### *Stroke*

A review summarized 49 studies from 84 post-stroke care clinical practice groups and treatment guidelines from 27 countries between 2001 and 2021 and described acupuncture for 15 symptom areas after stroke, such as stroke rehabilitation, dysphagia, and shoulder pain, which gave positive recommendations for the use of acupuncture [52]. The possible processes by which stem cell therapies and acupuncture may bridge the gap between contemporary, developing stem cell therapies and conventional acupuncture were detailed in a prospective review, and their potential advantages for better clinical results were highlighted [53]. At the cellular and molecular levels, this research compares traditional acupuncture with contemporary, developing stem cell treatments and highlights their potential advantages for better clinical outcomes. As for mechanistic studies, acupuncture stimulates neurogenesis, activates axonal regeneration and sprouting, and improves synaptic structure and function, thereby altering the neural network and function of damaged brain areas, promoting function and adaptability [54]. ISSA-MS6-i, ISSA-MS7-i, ISSA-PR, SAPL-Ex.HN3, and SAPL-GV20, SAPL-GV24 can be regarded as a crucial scalp acupuncture site combination for the administration of hemiplegia after stroke, based on a systematic review that examined the effectiveness of scalp acupuncture in treating patients with hemiplegia after stroke [55].

In a landmark study, acupuncture reduces spinal hyperreflexia and motor impairment via KCC2-mediated spinal GABAA activation in rats with spastic hypertension following ischemic stroke [20]. The synergistic effects of acupuncture in combination with Naomaitong in ischemic stroke were clarified by integrating 16S rRNA gene sequencing and liquid chromatography-mass spectrometry metabolomics [22]. Neuroimaging evidence contributes to a better understanding of how electroacupuncture works to treat ischemic stroke by localizing in the sensorimotor network, interoceptive network, default mode network, and salience network [23].

In clinical trials, a score-matched cohort study of acupuncture interventions in stroke patients at risk for dysphagia showed positive results [24]. Another population-based cohort study has shown that acupuncture-assisted treatment reduces long-term mortality in stroke patients [25].

### *Depression*

A meta-analysis reported that acupuncture or acupuncture combined with antidepressants was strongly linked to lower Hamilton Rating Scale for Depression scores with strong evidence [26], and another reported the effectiveness of acupuncture on postpartum depression [27]. The results of the meta-analysis of concomitant or residual insomnia showed that acupuncture exhibited a small therapeutic benefit over sham/placebo acupuncture for insomnia as a lingering symptom of previously or partially remitted depression, while it was equivalent to conventional therapy in decreasing Pittsburgh Sleep Quality Index scores across all categories [28].

A basic study found that electroacupuncture prevented depressive-like behavior by suppressing the NF-κB/NLRP3 inflammatory pathway in the hippocampus of mice exposed to chronic mild stress [29], and that acupuncture improved depressive behavior by modulating hippocampal Iba-1 and high mobility group protein expression in rats subjected to chronic restraint stress [30].

Results of a randomized clinical trial showed that electroacupuncture improved sleep quality in depressed patients, which was evident at week 8 and sustained to week 32 [31].

### *Cancer*

Several reviews related to acupuncture for cancer treatment have been conducted. Acupuncture has been shown to help with cancer-related pain, fatigue, insomnia, nausea and vomiting, bone marrow suppression, menopausal symptoms, arthralgia, dysphagia, and cancer patients' quality of life [32, 40]. The effectiveness and security of acupuncture and auricular acupuncture for cancer survivors with sleep disturbances were evaluated, and the outcome affirmed acupuncture acted as a safe intervention, while no evidence was found regarding the short-term or long-term effects of acupuncture or auricular acupuncture in improving sleep disorders in cancer survivors [33]. Several types of research have shown that acupuncture provides numerous advantages. in terms of CRF when compared to sham acupuncture, treatment as usual care, or wait-list control [34]. In addition, acupuncture is a promising intervention for both post-surgery and post-chemotherapy patients, and it should be recommended as a useful alternative strategy to facilitate the application of adult lung cancer patient-reported outcomes at all stages for patients with lung cancer [35].

Acupuncture studies on fatigue-like behavior, intestinal microbiota,

intestinal inflammatory and neuroinflammatory responses, intestinal barrier, hypothalamic-pituitary-adrenal axis, and altered serum metabolomics in mice producing CRF after chemotherapy for breast cancer found that moxibustion treatment can alleviate fatigue and improve the intestinal barrier, intestinal inflammation, neuroinflammation, and hypothalamic-pituitary-adrenal axis dysfunction in mice with CRF after chemotherapy [37].

The efficiency gains analysis of acupuncture, capecitabine plus paclitaxel, neoadjuvant chemotherapy, and radiotherapy for progressive gastric cancer, which confirmed the certain effect of acupuncture on recovery from acute toxicity after radiotherapy in advanced gastric cancer patients, was one of the few clinical studies with high impact factors currently available [38]. The consequences of several randomized controlled trials have shown that acupuncture can relieve symptoms associated with chemotherapy-induced peripheral neuropathy during oncology treatment [36]. Moreover, it can improve the structural regeneration of chemotherapy-induced peripheral neuropathy, especially in terms of subjective improvement and neurological effect [56]. And acupuncture combined with antiemetics can reduce the incidence of postoperative adjuvant chemotherapy-induced nausea and vomiting, enhance the level of living standards for patients, and decrease the likelihood of unfavorable side effects of antiemetics [39].

### *COVID-19*

Transcutaneous auricular vagus nerve stimulation is a healer for depressive symptoms on the COVID-19 assessment because it promotes immune function through cholinergic anti-inflammatory pathways and modifies brain circuits via the hypothalamic-pituitary-adrenal axis. Transcutaneous auricular vagus nerve stimulation therapy for COVID-19-related multi-organ damage and depressive symptoms may have as a possible target the interaction between brain circuits and anti-inflammatory mechanisms [57]. A review that summarized the evidence, guidelines, and consensus recommendations for acupuncture therapy, prevention, and rehabilitation of patients with COVID-19 in 2019 revealed that acupuncture was effective in treating these individuals [58].

One randomized controlled trial has shown that cupping and acupuncture were safe and effective treatments for COVID-19, which may provide a solution for COVID-19's upcoming care [41].

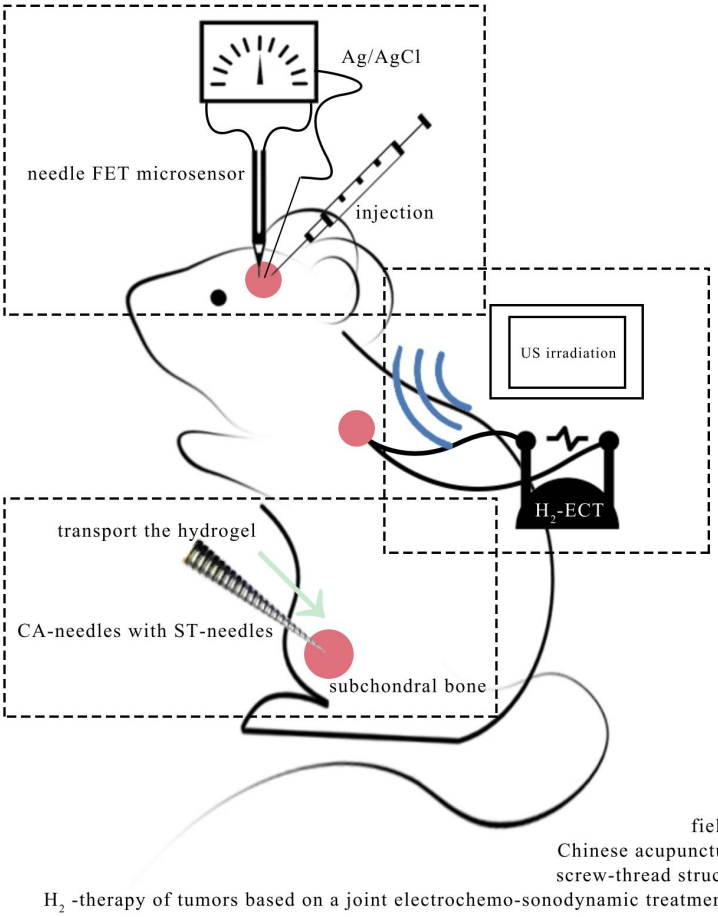
### *Others*

In a review of acupuncture for hematologic malignancies and hematopoietic cell transplantation, the current evidence for acupuncture treatment and the mechanism of action were summarized, and the evidence showed that acupuncture was beneficial to pain, nausea, and vomiting promotion, however, the effectiveness for peripheral neuropathy, fatigue, constipation, insomnia, night sweats, and pruritus were still unclear [59]. In a review of acupuncture modulation of inflammation at specific acupuncture point ST36 and its underlying mechanisms summarized in a study, it was demonstrated that acupuncture at ST36 was clinically beneficial in controlling inflammation through a variety of approaches, including vagal activation, TLR4/NF-κB signaling, macrophage polarization, the mitogen-activated protein kinase signaling pathway, and the cholinergic anti-inflammatory pathway [60]. A meta-analysis by Cochrane provided weak evidence that acupuncture, compared to medication, may improve or cure overactive bladder symptoms and decrease the frequency of mild side effects [42]. A comprehensive meta-analysis of rheumatoid arthritis treatments found that electroacupuncture combined with disease-modifying anti-rheumatic drugs (DMARDs) was the most effective combination of treatments for increasing DAS28 values, while fire acupuncture combined with DMARDs and moxibustion combined with DMARDs was the best combination therapy for improving pain and serological indicators. A meta-analysis evaluating the effects of acupuncture on respiratory disease in rodent models affirmed the therapeutic role of acupuncture as a possible treatment for respiratory disease by modulating various cytokines, leading to a reduction in inflammation [44]. The foundation of acupoints as response sites for acupuncture is the enrichment of mast cells and the relative vicinity of collagen fibers, microvessels, and nerves, and acupuncture can deform collagen fibers and activate transient potential receptor vanilloid channels on mast cell membranes, stimulating mast cells to release bioactive substances and activating nerve receptors to produce analgesic effects [61]. The force and torque generated by acupuncture manipulation indirectly activate mast cells through the collagen network, and as a result, different mediators, such as histamine, 5-hydroxytryptamine, adenosine triphosphate, and adenosine, are released from activated mast cells into the interstitial space. This was experimental evidence that subepidermal mast cells are involved in the triggering mechanism of acupuncture-induced analgesia. They then produce analgesic effects by activating local nerve terminals in peripheral ganglion sensory neurons that correspond to receptors in the local nerve terminals of peripheral ganglion sensory neurons [62]. It was also revealed that just a tiny portion of results from systematic reviews of acupuncture for adult health conditions were deemed to have high- or moderate-certainty evidence, with the vast majority of these including comparisons with sham therapy or concluding that acupuncture had no benefit [63].

It was proposed a post-traumatic stress disorder model combining a dialogue-based technique with physical manipulation via acupuncture, combining retrieval of traumatic memories with acupuncture to explain the described case study's positive Results [64]. The basic experiment demonstrated that acupuncture needles with a screw-thread structure at the tip (ST-needle) are used in osteoarthritis rats to conduct precise positioning in the subchondral bone, which impedes abnormal subchondral bone remodeling and lessens cartilage degeneration and degradation. This finding can be expanded for use in clinical precision positioning therapy [45]. A new surface-enhanced Raman scattering strategy was designed for the objective detection and monitoring of miRNA-21-5p in living cells and in vivo cerebrospinal fluid by applying hairpin DNA (hpDNA)-conjugated gold nanostars surface-enhanced Raman scattering probes, and acupuncture-based techniques [65] Yang et al. found that electroacupuncture attenuated surgical pain-induced delirium-like behavior in mice by remodeling the gut microbiota and dendritic spines, restoring the balance of the gut microbiota, preventing microglia activation, and reversing the elimination of dendritic spines, hence exposing a potential treatment strategy using patient perioperative electroacupuncture stimulation to prevent and/or treat surgical delirium [46]. In an animal study, through acupuncture for a rat intervertebral disc degeneration model, the confirmation of the activation of cannabinoid type 2 receptor delayed the reduction of intervertebral disc height, loss of nucleus pulposus water content, loss of nucleus pulposus cell and degradation of extracellular matrix caused by acupuncture. This research confirms that cannabinoid type 2 receptor is a crucial molecular target for delaying or even reversing intervertebral disc degeneration [47].

In this pilot, randomized clinical trial about irritable bowel syndrome, acupuncture in both the specific acupoints and nonspecific acupoints groups demonstrated clinically considerable improvement in irritable bowel syndrome with diarrhea symptoms [48]. One study also found that acupuncture was a promising treatment for anxiety in patients with Parkinson's disease, which suggested that acupuncture may improve the well-being of Parkinson's disease and anxiety patients [49].

In the development and application of needling sensors, it is reported that a powerful "domino effect" is generated by endogenous $H_2$ creation at tumor locations, combined electrochemo-sonodynamic treatment ($H_2$ -EC/SD co-therapy), and imaging-guided/assessed $H_2$ therapy of tumors that rapidly eliminates tumor tissue ($\leqslant$ 80 $mm^3$) in just one day [66]. In addition, a novel acupuncture needle-based field-effect transistor microsensor is proposed that is exceptionally sensitive and selective for monitoring neurotransmitters produced in rat brain real-time time, even in Parkinson's disease [67] (Figure 6).




field-effect transistor (FET)
Chinese acupuncture needles (CA-needles)
screw-thread structure needles (ST-needle)
$H_2$ -therapy of tumors based on a joint electrochemo-sonodynamic treatment ($H_2$ -EC/SD cotherapy)

**Figure 6 Study sites and patterns of needling sensors.** Transporting hydrogel via Chinese acupuncture needles was studied in humans.

***Conclusion***

The increasing number of reviews, basic studies, and clinical trials affirming the positive effects of acupuncture in the treatment of disease suggests that acupuncture is receiving more attention in the academic community, and that research on it is not limited to somatic or neuroinflammatory-related pathologies. Research on the application of acupuncture combined with sensors such as $H_2$ -EC/SD co-therapy, precise positioning, and vivo monitoring of neurotransmitters has provided newer and more scientific ways of treating diseases with acupuncture and has been explored in the areas of oncological diseases, neuropathic pain, and rehabilitation. In addition, with the global prevalence of COVID-19, its complications and associated symptoms are of great interest, and perhaps acupuncture can still play a positive role in regulating the body in this and other disease explorations.

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