

# Multimodal and data-driven approaches in acupuncture research: methods, applications, and challenges

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## Abstract

Acupuncture research increasingly involves heterogeneous and multimodal data that are difficult to analyze using conventional methods. This review summarizes data-driven approaches in acupuncture research within a framework encompassing intervention, response, and contextual data. We discuss causal inference, artificial intelligence, text mining, and integrative analysis, along with their applications in efficacy evaluation, outcome prediction, mechanistic investigation, and clinical decision support. These approaches shift the focus of acupuncture research from population-level average effects toward individualized clinical decision-making by enabling the analysis of treatment heterogeneity and underlying mechanisms. However, current research remains limited by inadequate data standardization, insufficient external validation, and limited model interpretability. Despite these challenges, data-driven approaches offer substantial promise for advancing more rigorous and personalized acupuncture research.

**Keywords:** Acupuncture, Causal inference, Clinical decision support, Data-driven, Deep learning, Machine learning, Mechanistic studies, Multimodal data

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## Introduction

As an important component of traditional Chinese medicine (TCM), acupuncture has been widely applied in pain management and neurorehabilitation, with increasing acceptance in international clinical practice<sup>[1–2]</sup>. Acupuncture is often described as exerting a holistic regulatory effect. In modern biomedical terms, this concept may involve coordinated influences on multiple targets and biological processes rather than a single pathway<sup>[3]</sup>. These mechanisms may contribute to interindividual variability and nonlinear treatment responses.

Earlier acupuncture research primarily addressed a fundamental question: does acupuncture produce benefits beyond placebo? These hypothesis-driven studies focused on a limited number of pre-specified outcomes

or biomarkers and relied on classical statistical methods to test average effects at the group level<sup>[4]</sup>. More recently, the focus has shifted from “whether acupuncture is effective” to “why acupuncture is effective” and “for whom acupuncture is effective.” This shift has prompted researchers to use richer datasets and more flexible analytical methods to capture heterogeneity in treatment response<sup>[5]</sup>. Advances in data acquisition technologies have expanded the scale of acupuncture research, facilitating the integration of multimodal data, including neuroimaging, physiological monitoring, and omics profiles<sup>[6]</sup>. Such multimodal data are often characterized by high dimensionality, complex correlations, and substantial heterogeneity<sup>[6–7]</sup>. These characteristics frequently violate the assumptions underlying traditional analytical methods. Consequently, data-driven approaches, such as

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machine learning (ML) algorithms that can accommodate high-dimensional data, nonlinear relationships, and complex dependency structures, have increasingly been introduced into acupuncture research<sup>[8]</sup>. Nevertheless, a systematic review addressing the applicability, interpretability, and clinical relevance of these diverse data-driven approaches in acupuncture research remains lacking.

In response, this review summarizes data-driven approaches used in acupuncture research and discusses their applications (Figure 1). We searched PubMed, Embase, Web of Science, CNKI, Wanfang Data, and VIP for studies published up to December 2025 using search terms related to acupuncture interventions and data-driven methods. Studies with clearly defined analytical frameworks were prioritized to provide a balanced evaluation of both strengths and limitations. This review aims to facilitate a shift from population-level average treatment effects toward more individualized acupuncture strategies for clinical decision-making.

### Multimodal data types in acupuncture research

In acupuncture research, multimodal data refer to information collected from different sources for the same subject or during the same intervention process and can be categorized into intervention, response, and contextual data (Table 1).

Intervention data describe the input characteristics of acupuncture interventions, including needle insertion depth and angle, stimulation frequency, retention time, and acupoint selection and localization<sup>[9]</sup>. These data have been used in previous studies to explore acupuncture dose–response relationships<sup>[10–12]</sup>; however, they are often influenced by practitioner-related variability, leading to inconsistent encoding across studies<sup>[13]</sup>.

As the response component in dose–response relationships, response data capture the effects of acupuncture on

clinical outcomes and multimodal biological processes. The scope of response data ranges from structured, low-dimensional measures, such as symptom scores and safety endpoints, to unstructured, high-dimensional data, such as neuroimaging, electrophysiological recordings, physiological signals, and omics profiles<sup>[14–17]</sup>. Analytical challenges arise from substantial differences in structure, scale, and temporal organization among these response data types<sup>[18]</sup>.

Contextual data complement intervention and response data by elucidating variability in acupuncture effects. These data include TCM diagnostic information, such as tongue and pulse assessments, as well as patient characteristics, treatment settings, and cultural expectations<sup>[19–20]</sup>. However, these data are often recorded in unstructured or semistructured formats and involve complex semantics and subjective interpretations<sup>[21]</sup>. These characteristics limit their direct integration into conventional quantitative analytical frameworks. Consequently, the primary analytical challenge lies in transforming contextual information into quantifiable variables through appropriate feature representation and text-mining techniques.

Multimodal data provide a multidimensional foundation for evaluating acupuncture effects and exploring underlying mechanisms; however, their heterogeneity complicates integration and analysis<sup>[8]</sup>. To address the two core questions of “why it works” and “for whom it works,” it is necessary to select analytical strategies capable of addressing this heterogeneity and managing unstructured contextual information.

### Data-driven analytical methods in acupuncture research

Causal inference methods enable acupuncture research to examine complex data more rigorously, moving beyond correlation to estimate causal effects.

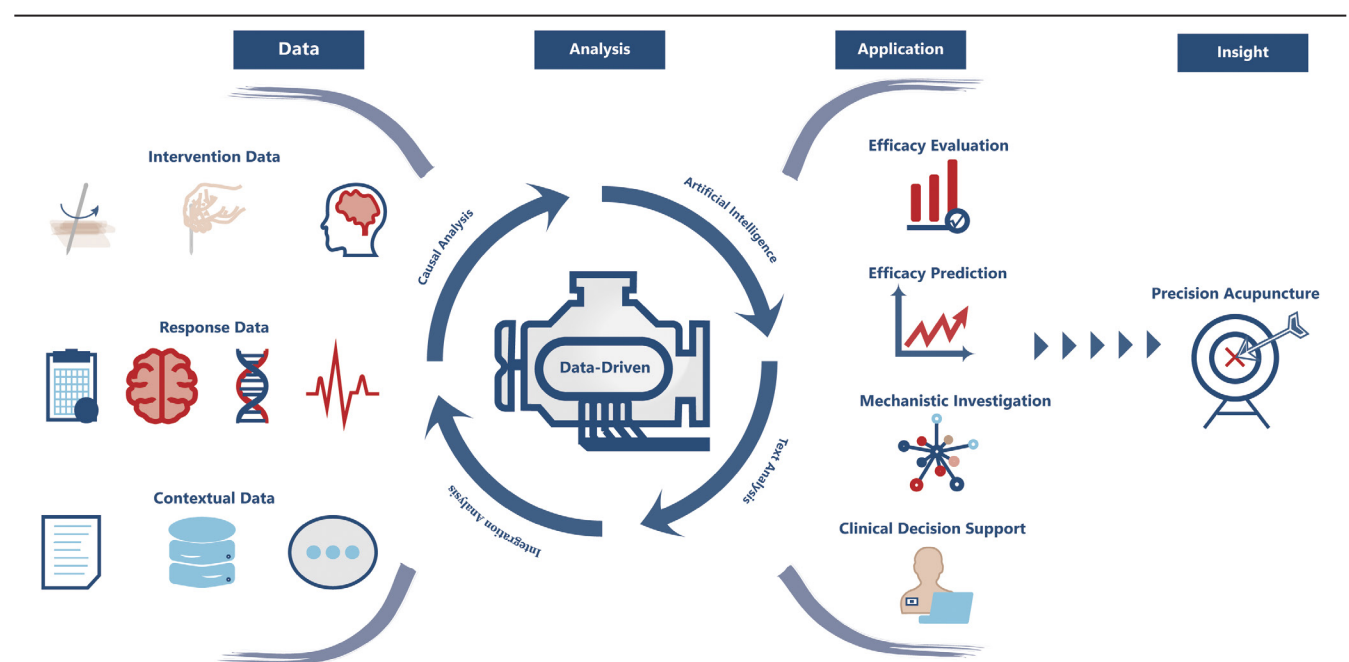


Figure 1. From data to precision acupuncture.

**Table 1**  
**Categories and characteristics of multimodal data in acupuncture research**

| Data type         | Subcategories                                    | Typical examples                                                                                                                    | Key features                                                                                                | Analytical implications                                                                            | Challenges                                                                                 |
|-------------------|--------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------|
| Intervention data | Acupoint prescription and operational parameters | Acupoint selection/ localization, needling depth/angle, stimulation frequency/intensity, needle retention time, etc.                | Mixed quantitative and categorical procedural data; basis for treatment fidelity and dose–response modeling | Support dose–response analysis, treatment standardization, and reproducibility assessment          | Practitioner variability; incomplete reporting; inconsistent terminology and data encoding |
| Response data     | Clinical outcomes                                | Patient-reported: VAS, PSQI, etc. Clinician-assessed: NIHSS, mRS, etc. Hard endpoints: adverse events, mortality, etc               | Direct therapeutic effect indicators                                                                        | Provide primary endpoints for efficacy evaluation; facilitate comparability across trials          | Subjectivity of scales; inconsistency across studies                                       |
|                   | Multimodal biomarkers                            | Neuroimaging, electrophysiology, physiological indicators, omics, etc                                                               | High-dimensional; multilevel mechanistic indicators                                                         | Support mechanism exploration and biomarker discovery                                              | Heterogeneous structure, scale, and temporal organization; complex data integration        |
| Contextual data   | Clinical and cultural metadata                   | TCM pattern differentiation, tongue and pulse assessments, patient characteristics, treatment settings, cultural expectations, etc. | Provide interpretive and cultural context; involve complex semantics and subjective interpretations         | Enable stratification by TCM syndrome; supplement interpretation of intervention and response data | Unstructured, semantically complex, low standardization                                    |

mRS: Modified Rankin Scale; NIHSS: National Institutes of Health Stroke Scale; PSQI: Pittsburgh Sleep Quality Index; TCM: Traditional Chinese Medicine; VAS: Visual Analog Scale.

Causal analysis

Causal inference advances acupuncture research from descriptive correlation to causal effect estimation. In research settings such as multicenter studies, longitudinal follow-up studies, real-world studies, and small sample investigations, traditional analytical methods often exhibit limitations, whereas causal inference approaches are better suited to addressing data complexity.

Modeling strategies for causal estimation

Multicenter and longitudinal acupuncture data are often hierarchical and time-dependent<sup>[22]</sup>. Traditional regression models tend to overlook between-center variability and within-individual correlation. Mixed-effects models, such as the generalized linear mixed model (GLMM), are designed to incorporate fixed effects, hierarchical structure, and temporal correlation, thereby producing more valid statistical inference<sup>[23–24]</sup>.

In small samples with substantial heterogeneity or non-normal outcomes, Bayesian approaches may yield more stable estimates by incorporating prior information and hierarchical structures. These approaches also provide posterior distributions that support probabilistic interpretation of treatment effects and associated uncertainty<sup>[25]</sup>. From longitudinal analyses in clinical trials to causal modeling in imaging-based mechanistic studies, these models have demonstrated substantial value<sup>[26]</sup>. Hierarchical Bayesian models allow simultaneous estimation of effects at the individual and population levels, which aligns with the individualized treatment principles central to acupuncture practice<sup>[27]</sup>.

Causal inference approaches

In real-world and observational acupuncture studies, causal inference commonly relies on propensity

score matching (PSM) and difference-in-differences (DID) methods. PSM reduces confounding arising from observed baseline differences, as demonstrated in a prospective cohort study addressing nonrandom treatment allocation<sup>[28]</sup>. DID compares changes in outcomes over time between exposed and unexposed groups and, if the parallel trends assumption holds, differences out time-invariant unmeasured confounding<sup>[29]</sup>. Although both methods can reduce bias, their validity depends heavily on matching procedures, sample selection, and modeling assumptions. Tleyjeh et al.<sup>[30]</sup> noted that implementation choices in PSM may undermine reproducibility. Shiba and Kawahara<sup>[31]</sup> further argued that poorly executed matching can introduce bias and reduce efficiency.

To address ambiguous causal questions and inconsistent temporal alignment in observational research, Hernan and Robins<sup>[32]</sup> proposed the target trial emulation (TTE) framework. TTE reconstructs key design features of an ideal randomized controlled trial (RCT) using claims data or electronic health records and has recently been applied in real-world studies of TCM, including investigations of Chinese herbal medicine in oncology and hypertension<sup>[33–35]</sup>.

Directed acyclic graphs (DAGs) formalize causal assumptions and identify appropriate adjustment strategies through the back-door criterion and, in some cases, clarify the assumptions underlying front-door or instrumental variable approaches<sup>[36]</sup>. In RCTs, in which controversies regarding control interventions and blinding are common<sup>[37]</sup>, DAGs may facilitate systematic identification of potential confounders and sources of bias once the causal estimand—such as the total or direct effect—has been clearly specified.

Dynamic causal modeling (DCM) is grounded in a physiological state-space model that estimates effective connectivity among brain regions through Bayesian model comparison and characterizes how acupuncture modulates neural network dynamics<sup>[38–39]</sup>. Its causal

interpretation, however, is restricted to directional dependencies specified within the model and is more appropriately understood as evidence of mechanistic coupling rather than of clinical causal effects<sup>[38]</sup>.

In summary, addressing causal questions in acupuncture studies requires the combined application of multiple methods: mixed-effects models to accommodate complex data structures, Bayesian methods to address small samples, PSM and DID to control confounding, TTE frameworks to standardize study design, DAGs to define causal hypotheses, and DCM to explore neural mechanisms.

### Artificial intelligence

When traditional statistical methods encounter limitations, artificial intelligence (AI) approaches can accommodate the high-dimensional, heterogeneous, and multimodal data common in acupuncture studies<sup>[8]</sup>.

### Machine learning

ML in acupuncture research can be categorized into supervised, unsupervised, and reinforcement learning<sup>[40]</sup>.

Supervised learning operates on labeled data and contributes to efficacy prediction, diagnostic support, and patient stratification in acupuncture research<sup>[41]</sup>. Different supervised models serve distinct analytical purposes. Support vector machines (SVMs) perform well in high-dimensional, small sample settings and are useful for distinguishing responders from non-responders and identifying predictive neuroimaging or deqi-related features<sup>[42–43]</sup>. Linear models, including logistic regression, offer greater interpretability and are commonly used to examine clinical and demographic variables and evaluate associations between treatment factors and outcomes<sup>[44]</sup>. Although regularization techniques such as the least absolute shrinkage and selection operator (LASSO) improve model stability by addressing multicollinearity and high dimensionality in linear models, tree-based methods—including decision trees and ensemble variants such as random forests and gradient boosting—provide advantages in modeling complex, heterogeneous data when linear assumptions are violated<sup>[40]</sup>. These models have been applied to RCTs and observational datasets to identify patient characteristics and intervention factors associated with treatment response; however, ensemble methods typically trade interpretability for predictive performance<sup>[45–46]</sup>.

Unsupervised learning is typically employed to identify latent structures and reduce dimensionality; it does not require labeled outcomes<sup>[41]</sup>. Examples include principal component analysis (PCA), which extracts features from neuroimaging and physiological data<sup>[47]</sup>. Acupuncture prescription records have also been analyzed using association rule mining, including the Apriori algorithm, which identifies high-frequency acupoint combinations and compatibility patterns to support prescription optimization<sup>[48]</sup>.

Reinforcement learning focuses on adaptive decision-making through interaction with the

environment and reward-based feedback<sup>[41]</sup>. Its application in acupuncture remains limited; however, preliminary studies in TCM have explored deep reinforcement learning for herbal prescription recommendation, suggesting potential future applications in acupuncture decision support systems<sup>[49]</sup>.

### Deep learning

Deep learning (DL) relies on multilayer neural networks to learn representations directly from raw data and is well-suited to the unstructured and multimodal data commonly encountered in acupuncture research, particularly imaging, physiological signals, and text data<sup>[50]</sup>.

Convolutional neural networks (CNNs) automatically capture local spatial features and are particularly suitable for imaging and other visual data. CNNs have demonstrated utility in analyzing brain activation patterns, quantifying diagnostic features in tongue and pulse examinations, and supporting acupoint localization and procedural monitoring through image or video analysis<sup>[51–55]</sup>.

Time-series and procedural data are often analyzed using recurrent neural networks (RNNs), long short-term memory (LSTM) networks, and transformer models. These methods can model needling manipulation signals—such as lifting, thrusting, and rotation—as well as electroencephalography (EEG) data to characterize temporal changes associated with acupuncture interventions<sup>[13,56]</sup>.

In small sample studies and representation learning tasks, variational autoencoders, a class of generative models, have been explored for feature extraction and signal reconstruction in EEG datasets<sup>[57]</sup>. They can also support data augmentation, which may partially mitigate sample size limitations, although careful validation is required.

In addition, the need to model complex relational and network-structured data has motivated exploratory applications of graph neural networks (GNNs) in acupuncture research. Existing studies have applied GNNs to represent network relationships among acupoints, meridians, and symptoms; to identify topological characteristics of frequently used acupoint combinations; and to interpret the systemic regulatory effects of acupuncture from a network-based perspective<sup>[58–59]</sup>.

Under conditions of small sample sizes and high-dimensional data, ML supports efficacy prediction, diagnostic assistance, patient stratification, and identification of acupoint compatibility patterns. DL has further expanded the capacity of acupuncture research to process unstructured data—including neuroimaging data, tongue and pulse images, needling manipulation signals, EEG recordings, and network representations of acupoints, meridians, and symptoms.

### Text analysis

Long-term acupuncture practice has generated a substantial body of textual material, including classical medical texts, case records, and contemporary literature. Because these texts are often experiential and nonstandardized, text analysis is required to uncover underlying patterns<sup>[60]</sup>.

### *Natural language processing*

Studies have demonstrated that natural language processing (NLP) can transform narrative descriptions of acupuncture into standardized representations to support the identification, standardization, and integration of key entities, such as acupoints and syndromes<sup>[61]</sup>. When combined with network analysis, NLP has been shown to reveal structural characteristics of acupoint compatibility patterns and to quantify clinical knowledge, thereby informing syndrome-based acupoint selection<sup>[62]</sup>.

### *Large language models*

Large language models (LLMs) represent an emerging approach to textual analysis within TCM<sup>[63]</sup>. Methodologically, they build on conventional NLP; the primary advancement is the transition from rule-based or manual feature extraction to representation learning based on large-scale corpora<sup>[40]</sup>. LLMs capture implicit semantic relationships, long-range dependencies, and complex contextual information in unstructured texts, thereby enhancing analysis of complex textual resources<sup>[21,64]</sup>.

### *Bibliometrics*

Because acupuncture research is widely dispersed across the literature, its overall trajectory is not always readily identifiable. Bibliometric analyses based on keywords, thematic clustering, and temporal trends can map the field's knowledge structure, track shifts in research priorities, and inform future directions<sup>[65]</sup>.

Several text analysis methods have been employed to process acupuncture-related textual data. NLP extracts key entities, such as acupoints and syndromes, from dispersed clinical records and transforms them into analyzable structured data; LLMs can identify implicit semantic relationships in ancient medical texts and records that are difficult to extract using rule-based approaches; and bibliometric analysis examines literature distribution and shifts in research topics to map the evolution of high-interest areas.

### *Integrative analysis*

Acupuncture response data are often multilevel, whereas a single data type typically captures only one aspect of treatment effects. Integrative analysis of multilevel data provides a more comprehensive understanding of the mechanisms underlying acupuncture.

### *Multi-omics integration*

Multi-omics integration combines information across different biological levels and can partially compensate for the limitations of single-omics analyses by facilitating observation of relationships among molecular changes<sup>[66–67]</sup>. In acupuncture research, several integrative strategies have been explored, including transcriptomics–metabolomics–metagenomics tri-integration and four-way integration of single-cell transcriptomics, bulk transcriptomics, metabolomics, and metagenomics<sup>[68–69]</sup>.

### *Neuroimaging integration*

Neuroimaging integration combines multiple types of brain imaging data<sup>[70]</sup>. Functional magnetic resonance imaging (fMRI) provides functional metrics, including regional homogeneity and functional connectivity, whereas structural magnetic resonance imaging characterizes anatomical properties, such as gray matter volume<sup>[71]</sup>. Integrating these modalities enables examination of the relationship between functional activity and structural substrates. Previous studies have employed regional homogeneity–functional connectivity–gray matter volume frameworks to elucidate the central mechanisms of acupuncture<sup>[72]</sup>.

### *Multimodal fusion*

Multimodal fusion integrates clinical outcomes with imaging data, physiological signals, and omics data, thereby providing more comprehensive information than any single modality alone<sup>[73]</sup>. In acupuncture research, studies have combined clinical outcomes with multimodal brain imaging to investigate how electroacupuncture modulates brain networks<sup>[72]</sup>. In cancer pain research, multimodal bioelectrical signal analysis has elucidated the neurophysiological mechanisms underlying acupuncture analgesia<sup>[47]</sup>. Beyond acupuncture, integration of EEG and multi-omics data has enabled accurate classification in related fields<sup>[74]</sup>.

Integrative analysis broadens research on acupuncture mechanisms by linking molecular changes, brain structure and function, and clinical or physiological responses. Compared with single modality analysis, integrative strategies facilitate a more comprehensive understanding of the acupuncture process and provide additional insights into differences in efficacy and individualized responses.

## **Applications in acupuncture research**

Building on the preceding overview of data characteristics and analytical methods in acupuncture research, this section examines their practical applications. Current applications primarily include efficacy evaluation, efficacy prediction, mechanistic investigation, and clinical decision support (Figure 2 and Table 2).

### *Efficacy evaluation*

To address repeated measurements and center-related variability in multicenter acupuncture trials, mixed-effects models are commonly employed. In a study by Yang et al.<sup>[23]</sup>, a GLMM was adopted to account for the longitudinal structure of response rate data (Table 2, No. 1). Lu et al.<sup>[24]</sup> modeled a methadone dose reduction of at least 20% from baseline using a GLMM and examined longitudinal changes in opioid craving using linear mixed-effects models. Both studies accounted for center effects, and Lu et al.<sup>[24]</sup> further included a center × intervention interaction term to assess whether treatment effects were consistent across centers. A Bayesian model with weakly informative priors was used in a randomized trial of acupuncture for chemotherapy-induced nausea to accommodate daily vomiting counts with

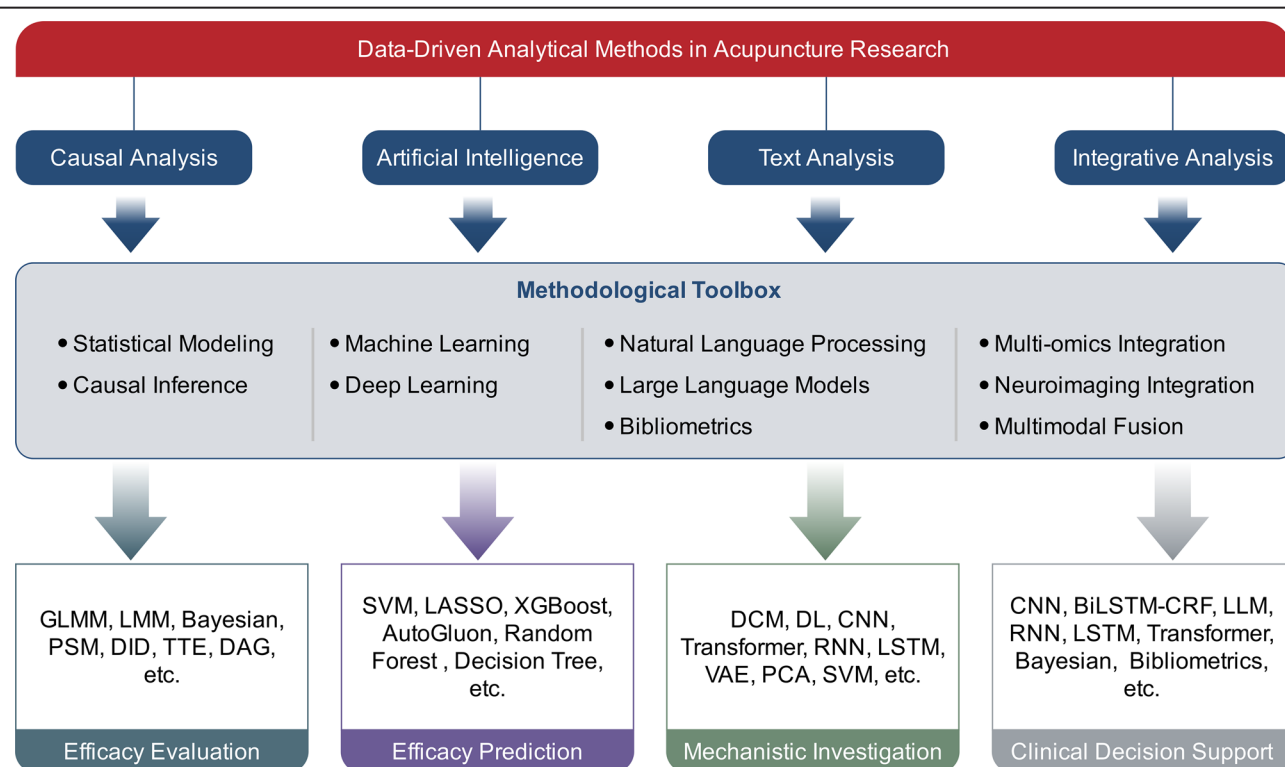


**Figure 2.** Mapping of analytical frameworks to applications in acupuncture research. BiLSTM-CRF: Bidirectional long short-term memory–conditional random field; CNN: Convolutional neural network; DAG: Directed acyclic graph; DCM: Dynamic causal modeling; DID: Difference-in-differences; DL: Deep learning; GLMM: Generalized linear mixed model; LASSO: Least absolute shrinkage and selection operator; LLM: Large language model; LMM: Linear mixed model; LSTM: Long short-term memory; PCA: Principal component analysis; PSM: Propensity score matching; RNN: Recurrent neural network; SVM: Support vector machine; VAE: Variational autoencoder; XGBoost: Extreme gradient boosting.

excess zeros<sup>[25]</sup> (Table 2, No. 2). The analysis indicated that acupuncture reduced vomiting during the first five days of treatment; however, the effect diminished rapidly after treatment cessation. This case illustrates the value of Bayesian methods in small samples with complex outcomes but also highlights their limited generalizability.

Causal inference methods have become increasingly common in real-world and observational studies of acupuncture. For instance, in chronic pain cohorts derived from electronic health records, patients receiving acupuncture were matched to those receiving conventional therapy using PSM (Table 2, No. 3), thereby reducing baseline confounding and improving comparability between groups<sup>[28]</sup>. Ng et al.<sup>[29]</sup> applied DID to evaluate the impact of acupuncture on analgesic use and healthcare utilization among breast cancer survivors (Table 2, No. 4). The results indicated that patients receiving acupuncture—particularly those treated for pain and those with higher treatment frequency—had fewer short-term analgesic prescriptions and lower medical costs than patients who did not receive acupuncture. After adjustment, however, these associations were no longer statistically significant. In parallel, a recent multicenter study applied TTE to evaluate Chinese herbal medicine in patients with stage IV non–small-cell lung cancer (Table 2, No. 5). The findings indicated that integrative Chinese herbal medicine use was associated with improved overall survival and cancer-specific survival, particularly when combined with epidermal growth factor receptor tyrosine kinase inhibitors<sup>[34]</sup>. Another real-world study that also applied TTE reported that Xuanshen Yishen Decoction

improved intensive blood pressure control and reduced readmission rates in patients with hypertension<sup>[35]</sup>.

No single method is suitable for all settings. Mixed-effects models are typically selected for hierarchical or longitudinal data, Bayesian methods for small samples or complex outcome distributions, and causal inference approaches for observational or real-world data. In acupuncture efficacy research, method selection should be guided by the research question and the structure of the data.

### Efficacy prediction

Patients do not respond uniformly to acupuncture. This variability has prompted efforts to identify responders, and AI methods have been explored for efficacy prediction.

In a multicenter RCT of functional dyspepsia (Table 2, No. 8), an SVM model based on routine clinical features achieved an accuracy exceeding 77% in predicting acupuncture responders and remained stable in an independent validation set<sup>[42]</sup>. Sex, disease subtype, and education level were identified as key predictive features in this study. In another study, SVM models were constructed using deqi characteristics recorded during the first acupuncture session to predict responder status and symptom improvement. The classification model achieved an accuracy of 84%<sup>[43]</sup>. The subjectivity of deqi assessment remains a limitation. Pre-treatment fMRI functional connectivity was also analyzed using an SVM model in patients with

**Table 2**  
**Comparative analysis of data-driven methods in acupuncture research: applicability, strengths, and limitations**

| No. | Category                | Specific method                 | Core principle and features                                                                           | Typical application scenarios in acupuncture                                                   | Advantages                                                                           | Limitations and critical challenges                                                          | Representative study (from article)                                                           |
|-----|-------------------------|---------------------------------|-------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------|
| 1   | Causal analysis         | Generalized linear mixed models | Models fixed and random effects to handle hierarchical or clustered data structures                   | Efficacy evaluation: multicenter RCTs with center effects; longitudinal repeated measures      | Handles center heterogeneity and within-subject correlation; yields stable estimates | Limited for high-dimensional biomarkers; relies on pre-specified linear assumptions          | Yang et al. <sup>[23]</sup> (multicenter trial for postprandial distress syndrome)            |
| 2   | Causal analysis         | Bayesian hierarchical models    | Combine prior information and observed data; model heterogeneity through hierarchical structures      | Small-sample, heterogeneous, longitudinal, or non-normal outcomes                              | Quantify uncertainty; support individual- and population-level estimation            | Computationally intensive; sensitive to priors and model assumptions                         | Ghosh et al. <sup>[25]</sup> (chemotherapy-induced nausea with zero-inflated daily data)      |
| 3   | Causal analysis         | Propensity score matching       | Balances observed baseline covariates between groups                                                  | RWE: comparative effectiveness using EHR/cohort data                                           | Reduces confounding from observed baseline differences; improves group comparability | Cannot address unmeasured confounding; sensitive to matching choices; may reduce sample size | Lindberg et al. <sup>[28]</sup> (EHR-based chronic pain cohorts)                              |
| 4   | Causal analysis         | Difference-in-differences       | Compares outcome changes between treatment and control groups over time                               | Pre-post observational studies of healthcare use or medication outcomes                        | Controls for unobserved confounders that are constant over time                      | Requires parallel trends; sensitive to time-varying confounding                              | Ng et al. <sup>[29]</sup> (impact of acupuncture on analgesic prescriptions in breast cancer) |
| 5   | Causal analysis         | Target trial emulation          | Designs observational analyses to emulate a hypothetical RCT                                          | RWE using claims data, EHR, or registries for large-scale effectiveness evaluation             | Clarifies causal estimands; helps reduce immortal time bias                          | Data quality dependence; requires precise definition of “time zero” and eligibility          | Lu et al. <sup>[34]</sup> (cited as a future framework for real-world acupuncture studies)    |
| 6   | Causal analysis         | Directed acyclic graphs         | Formalize causal assumptions and identify adjustment sets                                             | RCT design and analysis involving control interventions and blinding                           | Identify potential confounders and sources of bias; clarify causal estimands         | Depend on prior causal assumptions; misspecification may affect adjustment decisions         | Tennant et al. <sup>[36]</sup> (methodological application for minimizing bias)               |
| 7   | Causal analysis         | Dynamic causal modeling         | Infers effective connectivity (directional influence) among brain regions based on biophysical models | Neuroimaging mechanism: mapping causal flow in brain networks                                  | Provides model-based evidence of directional neural coupling                         | Computationally expensive; validity depends on the predefined anatomical model space         | Ma et al. <sup>[38]</sup> (electroacupuncture modulation of limbic-cortical feedback)         |
| 8   | Artificial Intelligence | Support vector machine          | Finds optimal hyperplanes to classify data points in high-dimensional space                           | Efficacy prediction: classifying responders vs. non-responders using clinical/imaging features | Suitable for small-sample, high-dimensional scenarios common in acupuncture research | Limited interpretability and requires careful validation                                     | Yin et al. <sup>[42]</sup> (predicting functional dyspepsia responders with >77% accuracy)    |
| 9   | Artificial intelligence | LASSO regression                | Uses L1 regularization to shrink some coefficients to zero                                            | Prognostic factor discovery: selecting key predictors from high-dimensional pools              | Sparsity leads to high interpretability; effectively screens redundant variables     | Selection instability when predictors are highly collinear; assumes linear relationships     | Kong et al. <sup>[75]</sup> (identifying prognostic features for chronic low-back pain)       |

(Continued)

**Table 2**  
(Continued)

| No. | Category                | Specific method                         | Core principle and features                                                        | Typical application scenarios in acupuncture                                                                      | Advantages                                                                              | Limitations and critical challenges                                                                    | Representative study (from article)                                                                                |
|-----|-------------------------|-----------------------------------------|------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------|
| 10  | Artificial intelligence | XGBoost/ Random Forest                  | Aggregates multiple decision trees to improve prediction accuracy and stability    | Complex clinical prediction: handling non-linear relationships and feature interactions                           | Outperforms single models in accuracy; handles missing values and non-linearity well    | High complexity; identifying the direction of effect for specific features is less intuitive           | Fu et al. <sup>[44]</sup> (predicting depression outcomes).                                                        |
| 11  | Artificial intelligence | Convolutional neural networks           | Extracts hierarchical spatial features <i>via</i> convolution layers               | Objectification: tongue/pulse diagnosis; fNIRS/ fMRI spatial pattern recognition                                  | Powerful automated feature extraction from images and signals; end-to-end learning      | Data-hungry; high risk of overfitting on small datasets; lack of spatial interpretability              | Khan et al. <sup>[51]</sup> (fNIRS classification)                                                                 |
| 12  | Artificial intelligence | RNN / LSTM network                      | Models sequential dependencies using recurrent connections and memory cells        | Temporal dynamics: analyzing time-varying EEG or physiological signals during acupuncture                         | Captures long-term temporal dependencies and dynamic evolution of signals               | Training difficulties; gradient issues; limited interpretability                                       | Li et al. <sup>[76]</sup> (reconstructing frontal cortex dynamics/attractors <i>via</i> recurrent neural networks) |
| 13  | Artificial intelligence | Transformer                             | Uses self-attention mechanisms to process sequential data in parallel              | Procedure recognition: distinguishing manipulation techniques (eg, twirling <i>vs.</i> retention)                 | Superior at capturing long-range dependencies; computationally more efficient than RNNs | Requires massive data for pre-training; high overfitting risk in small studies                         | Rao et al. <sup>[77]</sup> (acupuncture state detection at ST36 with ~85% accuracy)                                |
| 14  | Artificial intelligence | Variational autoencoder                 | Learns latent representations of high-dimensional data through generative modeling | EEG feature extraction, reconstruction, and augmentation                                                          | Enables representation learning and data augmentation                                   | Limited interpretability; validation required                                                          | Guo et al. <sup>[78]</sup> (discovery of low-dimensional neural subspaces/ attractors)                             |
| 15  | Artificial intelligence | Graph neural networks/ network analysis | Models relationships between nodes (entities) in a graph structure                 | Acupoint compatibility: mining rules of acupoint combinations and meridian networks                               | Aligns with the holistic/systemic nature of TCM theory; captures relational complexity  | Methodology is nascent in acupuncture; results depend heavily on how “edges” are defined               | Li et al. <sup>[58]</sup> (acupoint compatibility prediction)                                                      |
| 16  | Text analysis           | Natural language processing             | Computational processing of human language text (NER, relation extraction)         | Knowledge extraction: structuring acupoint indications from ancient/modern literature                             | Converts unstructured text into structured databases; enables large-scale mining        | High semantic ambiguity in TCM terminology; requires specialized ontologies                            | Lee et al. <sup>[62]</sup> (extracting acupoint location relations)                                                |
| 17  | Text analysis           | LLMs                                    | Large-scale corpus-based representation learning for unstructured texts            | TCM textual analysis: extracting semantic relationships and contextual information from complex textual resources | Captures implicit semantic relationships, long-range dependencies, and complex context  | Hallucination risk; domain-specific precision depends on fine-tuning, retrieval, and expert validation | Liu et al. <sup>[79]</sup> (Tianyi).                                                                               |
| 18  | Text analysis           | Bibliometrics                           | Quantitative analysis of publication metadata and citations                        | Trend analysis: visualizing research frontiers, hotspots, and academic networks                                   | Visualizes the evolution of the field; identifies emerging topics (eg, stroke rehab)    | Descriptive only; does not assess the quality or validity of the underlying evidence                   | Zhang et al. <sup>[80]</sup> (global trends in acupuncture for stroke)                                             |

(Continued)

**Table 2**  
(Continued)

| No. | Category             | Specific method         | Core principle and features                           | Typical application scenarios in acupuncture                                          | Advantages                                                                       | Limitations and critical challenges                                                     | Representative study (from article)                                                 |
|-----|----------------------|-------------------------|-------------------------------------------------------|---------------------------------------------------------------------------------------|----------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|
| 19  | Integrative analysis | Multi-omics integration | Combines genomics, transcriptomics, metabolomics, etc | Systemic mechanisms: elucidating cross-level pathways (eg, gut-microbiota-metabolism) | Overcomes single-omics limitations; reveals holistic biological networks         | Batch effects; difficult to match samples across layers; high cost and complexity       | Chen et al. <sup>[68]</sup> (methadone/microbiota)                                  |
| 20  | Integrative analysis | Imaging integration     | Combines fMRI and sMRI (sMRI/DTI) imaging data        | Central mechanisms: linking brain function changes to structural plasticity           | Validates functional findings with structural substrates; comprehensive CNS view | Complex registration/alignment of modalities; statistical multiple comparison issues    | Cao et al. <sup>[72]</sup> (ReHo-FC-GMV comparison of real vs. imagery acupuncture) |
| 21  | Integrative analysis | Multimodal fusion       | Fuses clinical, physiological, and omics data         | Phenotyping and prediction: leveraging complementary info for higher accuracy         | Maximizes information utilization; captures cross-modal interactions             | Data heterogeneity (time scales, formats); missing data challenges; modeling complexity | Han et al. <sup>[74]</sup> (EEG + multi-omics fusion for neurocognitive disorders)  |

CNS: Central nervous system; DTI: Diffusion tensor imaging; EEG: Electroencephalography; EHR: Electronic health record; fMRI: Functional magnetic resonance imaging; fNIRS: Functional near-infrared spectroscopy; LLMs: Large language models; NER: Named entity recognition; QA: Question answering; RAG: Retrieval-augmented generation; RCT: Randomized controlled trial; ReHo-FC-GMV: Regional homogeneity–functional connectivity–gray matter volume; RNN: Recurrent neural network; RWE: Real-world evidence; sMRI: Structural magnetic resonance imaging; ST36: Stomach 36 (Zusanli); TCM: Traditional Chinese Medicine.

neck pain. The classification accuracy reached 85%, and 117 connectivity edges were identified; however, only three remained significantly associated with pain visual analog scale scores after correction<sup>[81]</sup>. The small sample size and high dimensionality of the imaging data reduced the stability of the findings. Beyond SVM, LASSO regression has been applied in acupuncture research for feature selection in predictor-rich settings. In two parallel trials of electroacupuncture for chronic low-back pain (Table 2, No. 9), researchers used LASSO to identify prognostic features in the first trial and subsequently predicted patient-reported functional outcomes in the second; the cross-study applicability of the model was thereby demonstrated<sup>[75]</sup>. Similarly, in chronic prostatitis/chronic pelvic pain syndrome, LASSO was employed to select key predictors, which were incorporated into a nomogram that achieved good discriminative performance in both training and validation cohorts<sup>[82]</sup>. These studies suggest that LASSO facilitates the development of individualized prognostic tools by selecting clinically relevant predictors from high-dimensional data; however, its selection process may be unstable when sample sizes are limited or predictors are highly correlated<sup>[83]</sup>.

Tree-based models and ensemble learning methods demonstrate advantages in handling complex data relationships. In predicting treatment outcomes for major depressive disorder, researchers used structured, low- to medium-dimensional response data and demographic factors. Multiple algorithms were compared, and XGBoost achieved the best predictive performance, outperforming logistic regression, random forest, and SVM<sup>[44]</sup> (Table 2, No. 10). Similarly, in ischemic stroke with upper limb dysfunction, AutoGluon was used

to integrate clinical outcomes (National Institutes of Health Stroke Scale [NIHSS], Fugl-Meyer Assessment–Upper Extremity [FMA-UE], and Modified Barthel Index [MBI]) and multimodal biomarkers derived from digital subtraction angiography imaging, achieving accuracies of 77% to 88% and identifying middle cerebral artery and internal carotid artery stenosis sites as key predictors<sup>[84]</sup>. A limitation was that the study focused exclusively on large-vessel stenosis without considering microcirculation or collateral circulation. Decision tree analysis of methadone dose reduction and craving scores provided a strategy for addressing efficacy heterogeneity in acupuncture-assisted therapy<sup>[85]</sup>. The model identified opioid use duration and administration route as key factors; however, the relatively small training dataset and limited external validation constrained its stability and generalizability.

Rather than treating prediction solely as a binary classification task, ML methods have been used to uncover the underlying structure of treatment response. The emphasis has been on identifying which patient characteristics, clinical features, or multimodal biomarkers are most informative. Across different algorithms and data types, a recurring observation is that predictive performance often depends on a subset of interpretable features rather than on the full data dimensionality. This finding suggests that the value of ML in this context lies not only in predictive accuracy but also in its capacity to generate hypotheses regarding the determinants of individual response. Although the clinical applicability of these models remains to be established, they provide a methodological foundation for moving from population-level averages toward a more stratified understanding of acupuncture effects.

### Mechanistic investigation

Data analysis methods provide a distinct analytical direction in acupuncture research by facilitating mechanistic interpretation. Through causal analysis, AI, and integrative analysis, researchers can explore potential pathways underlying acupuncture interventions.

Ma et al.<sup>[38]</sup> combined task-based fMRI with DCM to examine electroacupuncture in neuropathic pain following brachial plexus avulsion (Table 2, No. 7). The analysis focused on corticolimbic circuits and found that electroacupuncture weakened connectivity from the hypothalamus and amygdala to S1, suggesting modulation of neural information flow and preliminary network plasticity.

AI has further advanced mechanistic exploration in acupuncture research. In a study analyzing EEG data during stimulation of the Zusanli (ST36) acupoint, Rao et al.<sup>[77]</sup> demonstrated that a CNN–Transformer model distinguished between twirling and retaining manipulations with an accuracy of approximately 85% (Table 2, No. 13). Brain topographic analysis indicated that these differences were associated with delta-band activity in the left frontal and parieto-occipital regions, highlighting that twirling and retaining manipulations are linked to distinct patterns of brain activity. Khan et al.<sup>[51]</sup> combined a CNN with functional near-infrared spectroscopy to investigate acupuncture in mild cognitive impairment (Table 2, No. 11). By recording prefrontal activity during working memory tasks, they observed that post-acupuncture reductions in between-group differences in brain activity may indicate normalization of prefrontal function. Although acupuncture is known to regulate physiological functions and cognitive processes, the mechanisms underlying different manipulations remain unclear. Li et al.<sup>[76]</sup> analyzed EEG recordings obtained during acupuncture stimulation at ST36 using RNNs (Table 2, No. 12). From a low-dimensional dynamical perspective, they examined how different manipulation techniques were represented in neural activity. The results demonstrated stable periodic attractor dynamics in the frontal cortical network during acupuncture, with technique-specific differences reflected in the interaction and separation of these attractors. Guo et al.<sup>[78]</sup> extended this approach by applying a variational autoencoder (VAE) to multichannel EEG signals recorded during stimulation at the ST36 acupoint (Table 2, No. 14). Their analysis revealed that acupuncture reduced the dimensionality of brain activity, giving rise to a low-dimensional neural subspace termed the “acupuncture mode.” This mode exhibited similar elliptical attractor structures across different subjects and was closely associated with enhanced oscillatory activity in the delta and alpha frequency bands. The attractor morphology also varied with stimulation frequency. One possible interpretation is that acupuncture constrains neural activity within a low-dimensional subspace to coordinate physiological outputs. All three studies investigated ST36 acupuncture using EEG and deep learning but with distinct emphases: Rao et al.<sup>[77]</sup> established that different manipulation techniques produce distinct, classifiable patterns of cortical activation; Li et al.<sup>[76]</sup> characterized these differences within a dynamical systems framework, demonstrating how techniques alter attractor dynamics,

and Guo and Wang<sup>[78]</sup> revealed that acupuncture constrains brain activity into a shared low-dimensional subspace whose structure varies with stimulation parameters. Collectively, these findings suggest that acupuncture at ST36 does not merely activate or suppress brain regions but reorganizes the dynamical landscape of cortical activity in a technique-specific manner.

Integrative analyses provide system-level insights through the synthesis of multilayered data. Omics integration revealed that electroacupuncture combined with tenofovir improved the intestinal barrier, increased taurine and all-trans retinoic acid levels, enriched beneficial bacteria, and regulated the peroxisome proliferator-activated receptor pathway, thereby potentially preventing viral replication<sup>[69]</sup>. In methadone maintenance patients (Table 2, No. 19), acupuncture reduced the required methadone dose. Multi-omics analyses from the same cohort further revealed immune regulation *via* the bile acid–Galectin-9–interferon (IFN)- $\gamma$  pathway and reversal of opioid-induced microbiota–metabolite alterations<sup>[68]</sup>. In spontaneously hypertensive rats, blood pressure decreased following both electroacupuncture and manual acupuncture, accompanied by shifts in gut microbiota composition and lipid and amino acid metabolism. In neuroimaging integration, studies comparing real acupuncture with video-guided acupuncture imagery treatment identified distinct neural pathways underlying analgesia. Real acupuncture more strongly activated the insula, whereas imagery treatment was associated with deactivation of the anterior cingulate cortex<sup>[72]</sup> (Table 2, No. 20). During acupuncture for cancer pain, a multimodal investigation employed portable sensors to monitor EEG and electromyography (EMG). The data were analyzed using PCA, time–frequency analysis, power spectrum analysis, and dynamic network analysis. The results showed that during needle retention, pain significantly decreased, EEG–EMG connectivity weakened, and signal power declined in stage-specific patterns<sup>[47]</sup>. These findings indicate that acupuncture may alleviate pain immediately through attenuation of functional coupling between central and peripheral systems. In neurocognitive disorders, integration of EEG, multi-omics data, and SVM modeling linked decreased EEG power spectral density to specific microbes (*Ruminococcus gnavus*) and metabolites (glutamate and  $\gamma$ -aminobutyric acid)<sup>[74]</sup> (Table 2, No. 21).

In summary, these approaches provide methodological support for extending acupuncture research from conventional efficacy evaluation toward mechanism-oriented exploration. They also promote a shift from single-modality observations toward multi-level, system-level perspectives on acupuncture-related effects.

### Clinical decision support

Traditional acupuncture decision-making has long relied on subjective physician experience; data-driven methods now complement this approach.

CNNs have advanced objective diagnosis in TCM through tongue inspection and pulse palpation. From tongue images, these models classify body and coating features to assist constitution and syndrome

differentiation<sup>[52,86]</sup>. In pulse diagnosis, they extract and classify waveform features, outperforming conventional approaches and demonstrating substantial potential for diagnostic objectification<sup>[55,87]</sup>.

In acupoint localization and prescription development, CNN-based object detection and segmentation models process visible light and infrared thermographic images, enabling automated acupoint recognition and real-time localization<sup>[56]</sup>. A GNN-based model integrating a feature-aware residual graph attention network with deep nonnegative matrix factorization identified previously undocumented acupoint combinations with potential therapeutic value<sup>[58]</sup> (Table 2, No. 15). These models have also enabled recognition and quantification of manipulation patterns<sup>[88]</sup>. A study on low back pain employed an improved mutual information method to construct acupoint compatibility networks (Table 2, No. 16). The networks revealed that combinations mainly consist of local and distal pairs, which can be further grouped into three distinct patterns: local points, meridian-based distal points, and syndrome-differentiated distal points<sup>[62]</sup>. In addition, relation extraction methods based on bidirectional long short-term memory–conditional random field models or LLMs have demonstrated feasibility in constructing acupoint–meridian–symptom networks<sup>[89]</sup>.

Acupuncture manipulation variability influences clinical efficacy; however, its teaching and learning still rely largely on personal experience rather than objective assessment. To address this limitation, researchers have combined CNNs with RNNs, such as LSTM networks, to analyze video or sensor data from acupuncture procedures<sup>[56]</sup>. These models have enabled recognition and quantification of manipulation patterns<sup>[88]</sup>. Rao et al.<sup>[77]</sup> proposed a Transformer-based detector that differentiated twirling from needle retention at ST36. With these tools, clinicians can monitor and quantify needle manipulation in real time. The objective data generated can help beginners practice against explicit benchmarks and allow instructors to correct manipulations more accurately, thereby supporting preservation and refinement of traditional skills through data-driven feedback.

LLMs are increasingly integrated with advances in objective diagnosis and structured knowledge to function as integrative tools for clinical decision support in acupuncture and TCM. Studies have evaluated general-purpose LLMs in diagnosis, syndrome differentiation, and acupoint selection<sup>[64]</sup>. The results indicated that GPT-4o, Qwen 2.5 Max, and Doubao 1.5 Pro showed high concordance with experienced acupuncturists on well-structured tasks. Their performance in more complex, TCM-specific decisions, however, remains variable. Specialized systems such as AcuGPT-Agent integrate acupuncture knowledge graphs with retrieval-augmented generation mechanisms to support disease-oriented decision-making in infertility<sup>[90]</sup>. In parallel, a TCM-specific foundation model (Table 2, No. 17), Tianyi, was pre-trained on diverse corpora to serve as a general knowledge backbone across clinical tasks<sup>[79]</sup>. Different categories of LLMs serve distinct roles in clinical decision support. At present, their primary function is to integrate diagnostic information, structured knowledge, and reasoning processes to assist clinicians.

Bibliometric tools such as CiteSpace and VOSviewer map the evolution of knowledge in acupuncture research, identifying frontier areas such as stroke rehabilitation<sup>[80]</sup> (Table 2, No. 18). These maps can be converted into structured knowledge representations to support automated updating of clinical guidelines and continuous refinement of decision-making rules.

The result is an integrated clinical decision support framework for acupuncture. CNNs, LLMs, bibliometric analysis, and related methods support objective diagnosis, manipulation quantification, knowledge integration, and evidence mapping, thereby facilitating a transition beyond reliance on subjective experience. As additional methods are incorporated, this framework may further enhance clinical decision-making.

### Considerations for data-driven acupuncture research

Although data-driven approaches have attracted increasing attention in acupuncture research, several practical challenges persist. A primary concern is the lack of standardization and substantial heterogeneity across datasets<sup>[8]</sup>. Problems arise in multiple domains, including inconsistent recording of intervention and contextual data and limited comparability of response data across studies<sup>[13,21,37,52,70]</sup>. These limitations hinder data integration, reduce reproducibility, and complicate cross-study validation. Such issues ultimately compromise the robustness and generalizability of subsequent analyses. Modeling presents additional challenges<sup>[8]</sup>. Many current models remain exploratory in nature. Although AI and causal inference methods have been applied to efficacy evaluation, efficacy prediction, mechanistic investigation, and clinical decision support, many studies continue to be constrained by small sample sizes, lack of external validation, and limited model interpretability<sup>[40–41,50,91]</sup>. These approaches require expertise across multiple disciplines, which further limits their practical implementation<sup>[92]</sup>. Consequently, many findings lack generalizability and are not yet ready for translation into clinical tools.

Overall, the major bottlenecks in current data-driven acupuncture research lie in data quality and standardization, methodological rigor, and clinical translation. At present, a mature pipeline linking data acquisition and analytical validation to clinical application has not been established. Future studies should place greater emphasis on data standardization, cross-center validation, development of interpretable models, and rigorous evaluation of models in specific clinical tasks<sup>[5,93]</sup>.

### Conclusions and prospects

Data-driven approaches are expanding acupuncture research from average-effect evaluation toward mechanism-informed and individualized investigation. These methods facilitate analysis of heterogeneous and multimodal data and enable examination of why acupuncture is effective and for whom it is most effective. However, current studies remain limited by insufficient data standardization, inadequate external validation, and restricted model interpretability. Future progress will depend on more standardized data collection, cross-center collaboration, and development of clinically

applicable analytical frameworks. Overall, data-driven research may provide an important foundation for more rigorous and personalized acupuncture research.

### Conflict of interest statement

The authors declare no conflict of interest.

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### Author contributions

Dehui Nie, Puchen Huang, and Dan Jin contributed equally to drafting the manuscript and conducting the literature review. Yiming Chen, Baochao Fan, and Shanshan Huang assisted with literature collection and data organization. Yuqing Zhang, Yu Zhou, Bin Han, and Jianlong Huang participated in manuscript review and editing. Gaolei Yao provided additional support in data analysis and manuscript preparation. Liming Lu and Peijing Rong supervised the study, critically revised the manuscript, and served as co-corresponding authors. All authors read and approved the final manuscript.

### Ethical approval of studies and informed consent

Not applicable.

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### Data availability

Data sharing is not applicable to this article because no datasets were generated or analyzed during the current study.

### Declaration of Generative AI in Scientific Writing

During the preparation of this manuscript, the authors used generative AI to assist with English language polishing, grammar correction, and improvement of readability. No generative AI was used for data analysis, interpretation of results, or drawing scientific conclusions. The authors reviewed and approved the final manuscript and take full responsibility for its content.

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