

# Clinical Review: Acupuncture for Treatment-Resistant Conditions

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## Abstract

Treatment-resistant conditions—such as treatment-resistant depression (TRD) and chronic pain refractory to conventional therapies—pose significant clinical challenges, often leading to persistent symptoms, reduced quality of life, and high healthcare costs. Acupuncture, a component of traditional Chinese medicine involving needle insertion at specific points to elicit therapeutic effects (including the *De-Qi* sensation of numbness, tingling, or heaviness), has emerged as a potential adjunctive or alternative therapy. This review synthesizes current evidence from randomized controlled trials (RCTs), observational studies, meta-analyses, and mechanistic research. While evidence quality varies (often low-to-moderate due to heterogeneity and blinding challenges), promising results support acupuncture’s role in symptom reduction, particularly when standard treatments fail, with a favorable safety profile.

## 1 Introduction

Treatment-resistant conditions are defined by inadequate response to evidence-based interventions (e.g.,  $\geq 2$  adequate antidepressant trials for TRD; failure of medications, physical therapy, or injections for chronic pain). These affect millions worldwide and contribute to disability and opioid overuse. Acupuncture’s mechanisms—neuromodulation, anti-inflammatory effects, and regulation of neuroendocrine pathways—make it a rational option for integrative care. Interest has grown in refractory cases where pharmacological side effects or limited efficacy create unmet needs. [7]

## 2 Mechanisms of Action

Acupuncture influences multiple pathways relevant to treatment-resistant states:

- **Neurotransmitter modulation:** Increases serotonin (5-HT) and other monoamines; correlates with symptom improvement in depression.
- **Anti-inflammatory and neuroplasticity effects:** Downregulates NF- $\kappa$ B, PI3K/AKT, and MAPK pathways; normalizes lipid metabolism and leptin resistance.
- **Autonomic and somatic regulation:** Balances sympathetic/parasympathetic activity; provides rapid relief of somatic symptoms (e.g., insomnia, pain) that often accompany psychiatric or chronic pain conditions.
- **Sensory gating:** *De-Qi* elicitation appears key, with pain sensitivity during needling sometimes predicting better outcomes.

These effects may be particularly beneficial in refractory cases involving intertwined physical and psychological symptoms. [6, 7]

### 3 Clinical Evidence by Condition

#### 3.1 Treatment-Resistant Depression (TRD) and Related Mood Disorders

Multiple studies and meta-analyses indicate acupuncture (manual, electro-, or specific protocols) as monotherapy or adjunct to antidepressants:

- A 2023 RCT of *Tiaoqi Jiayu* (regulating qi and relieving depression) acupuncture in 78 TRD patients showed a significantly higher response rate on the Hamilton Depression Rating Scale (HAMD-24) after 8 weeks: 52.8% (acupuncture group) vs. 17.1% (control/medication alone;  $P < 0.001$ ). Improvements in depression, anxiety (HAMA), and sustained follow-up effects were noted; symptom relief correlated with acupuncture-induced pain sensitivity changes. [1]
- A prospective single-arm study (n=36 TRD/bipolar disorder patients) using weekly acupuncture for 12 weeks reported early somatic symptom relief (neck pain, insomnia) and gains in psychiatric symptoms plus SF-8 quality-of-life subscales (bodily pain, general health, mental health). No worsening of bipolar features occurred. [3]
- Broader meta-analyses (including adjunctive use with SSRIs/SNRIs) show reductions in HAMD scores, higher response/remission rates, and fewer side effects compared to medication alone. Effects are often stronger as adjunctive therapy. [7]

Acupuncture appears especially useful for somatic comorbidities common in TRD.

#### 3.2 Treatment-Resistant Chronic Pain

Evidence is robust for musculoskeletal and other refractory pain:

- A 2025 prospective observational propensity-score-matched study (n=75 patients; median 18 months of pain unresponsive to conventional therapies) in Norwegian primary care used individualized *De-Qi* acupuncture (median 6 sessions). Pain (VAS) dropped from 6.2 to 3.2 at 12 months ( $P < 0.001$ ; large effect size). SF-36 scores improved markedly (moderate-to-large effects): 75% were strong responders ( $\geq 8$  T-score gain on physical component summary), 58% achieved complete “cure” (normal population health norms, PCS  $\geq 47$ ), and 17% near-normal. Benefits were dose-dependent ( $\geq 6$  sessions optimal) and held across ages, including elderly patients. No adverse events occurred. Propensity matching and Hill criteria supported causal inference. [2]
- Large individual-patient-data meta-analyses (e.g., Vickers et al.) of chronic pain (back, neck, shoulder, knee osteoarthritis, headache) confirm acupuncture’s superiority over no treatment and modest benefits over sham, with effects persisting  $\geq 12$  months. Real-world data align with these findings for refractory cases. [4, 5]

Other refractory pain syndromes (e.g., neuropathic, cancer-related, pelvic) show similar supportive trends in smaller reviews.

#### 3.3 Other Conditions

Limited but emerging data exist for drug-resistant epilepsy (adjunctive protocols), refractory insomnia in mood disorders, and certain auditory hallucinations in schizophrenia, though high-quality trials are scarcer.

## 4 Safety Profile

Acupuncture is generally well-tolerated. Adverse events are mild and transient (e.g., minor bruising, temporary soreness) and occur less frequently than with antidepressants. Serious events are rare when performed by trained practitioners using sterile single-use needles. No exacerbation of mania in bipolar patients has been reported in the cited studies. [3]

## 5 Limitations and Future Directions

- **Evidence quality:** Many trials are small, heterogeneous in protocols, and face blinding challenges (sham acupuncture is imperfect). Observational data (e.g., the Norwegian pain study) risk selection bias.
- **Generalizability:** Results often from East Asian or specific settings; practitioner expertise and *De-Qi* elicitation matter.
- **Gaps:** Few large, long-term RCTs focused exclusively on “treatment-resistant” definitions; cost-effectiveness and opioid-sparing data need expansion.

Future research should prioritize standardized protocols, larger multicenter RCTs, mechanistic imaging studies, and integration into guidelines for refractory cases.

## 6 Clinical Recommendations and Conclusion

For patients with TRD or refractory chronic pain failing standard care, acupuncture (especially adjunctive or *De-Qi*-focused) is a reasonable, low-risk option that may reduce symptoms, improve function/quality of life, and minimize medication side effects. A typical course involves 6–12 weekly sessions by a qualified practitioner, individualized to the patient’s pattern (e.g., specific points for depression or pain loci). It fits well in multimodal integrative care.

In summary, while not a panacea, acupuncture offers clinically meaningful benefits in selected treatment-resistant conditions, supported by growing real-world and trial data. It exemplifies the value of integrative approaches when conventional options are exhausted. Clinicians should discuss it with patients, weighing individual factors, and advocate for further rigorous research.

## References

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