

• Global Views

Acupuncture's Role in Solving the Opioid Epidemic: Evidence, Cost-Effectiveness, and Care Availability for Acupuncture as a Primary, Non-Pharmacologic Method for Pain Relief and Management—White Paper 2017

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ABSTRACT

The United States (U.S.) is facing a national opioid epidemic, and medical systems are in need of non-pharmacologic strategies that can be employed to decrease the public's opioid dependence. Acupuncture has emerged as a powerful, evidence-based, safe, cost-effective, and available treatment modality suitable to meeting this need. Acupuncture has been shown to be effective for the management of numerous types of pain conditions, and mechanisms of action for acupuncture have been described and are understandable from biomedical, physiologic perspectives. Further, acupuncture's cost-effectiveness can dramatically decrease health care expenditures, both from the standpoint of treating acute pain and through avoiding addiction to opioids that requires costly care, destroys quality of life, and can lead to fatal overdose. Numerous federal regulatory agencies have advised or mandated that healthcare systems and providers offer non-pharmacologic treatment options for pain. Acupuncture stands out as the most evidence-based, immediately available choice to fulfil these calls. Acupuncture can safely, easily, and cost-effectively be incorporated into hospital settings as diverse as the emergency department, labor and delivery suites, and

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neonatal intensive care units to treat a variety of commonly seen pain conditions. Acupuncture is already being successfully and meaningfully utilized by the Veterans Administration and various branches of the U.S. Military, in some studies demonstrably decreasing the volume of opioids prescribed when included in care.

Keywords: acupuncture; opioid epidemic; pain; opiate dependency; effectiveness; safety; cost-effectiveness; mechanism; United States

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1 Introduction

In 2015 it was estimated that 25.3 million Americans suffered from chronic pain, while an estimated 126 million American adults reported some type of pain in the prior three months.^[1] As a result, more than 240 million prescriptions were written for opioid medications during that year.^[2] An unfortunate consequence of this high use and availability of opioids, is a growing number of opioid-related deaths from addiction and overdose. More than 33 000 Americans died from opioid drugs in 2015, and more than 64 000 died in 2016.^[3] Due to the severity of this epidemic, a White House panel urged the United States (U.S.) president to declare the opioid crisis a national emergency, and August 31, 2017 was designated as “International Overdose Awareness Day” by the Centers for Disease Control and Prevention (CDC).^[4]

To cope with the opioid crisis, various federal regulatory and oversight agencies, including the U.S. Food and Drug Administration (FDA), the National Academies of Sciences, Engineering, and Medicine (NASEM), and the Joint Commission have started to advise or mandate that healthcare systems and providers offer non-pharmacologic treatment options for pain control.^[5–7] Acupuncture stands as the most evidence-based, immediately available choice to fulfil these calls.

The aim of this white paper is to summarize for academic scholars, healthcare professionals, administrators, policymakers, and the general public the available evidence for acupuncture as a treatment for various pain conditions as well as for opiate dependency. This includes evidence on the safety, cost-effectiveness, mechanisms of action, and provider availability for acupuncture.

2 Acupuncture is an effective, safe, and cost-effective treatment for numerous types of acute and chronic pain; acupuncture should be recommended as a first line treatment for pain before opiates are prescribed, and may reduce opioid use

2.1 Effectiveness/Efficacy of acupuncture for different types of pain

There is growing research evidence to support the

effectiveness and efficacy of acupuncture for the relief of numerous types of pain, especially chronic pain, as well as for the use of acupuncture for a diverse array of medical conditions. In an independently published work, which is the largest and most comprehensive of its kind for the period evaluated, McDonald and Janz^[8] summarized the research from March 2013 to September 2016 for acupuncture, published and available in all languages on PubMed and in the Cochrane Library. They looked at systematic reviews, meta-analyses, network meta-analyses, overviews of systematic reviews (NHMRC level I evidence), and a number of narrative reviews. They performed meta-analyses on 62 of the non-Cochrane systematic reviews, representing pooled data from more than 1 000 randomized controlled trials (RCTs). They assessed and graded the quality of evidence, and noted the strength of evidence for acupuncture for numerous conditions (Box 1, Appendix 1).

Acupuncture has been found to be effective for treating various types of pain, with the strongest evidence emerging for back pain, neck pain, shoulder pain, chronic headache, and osteoarthritis. In an individual patient meta-analysis of 17 922 people from 29 RCTs, patients receiving acupuncture had less pain, with scores that were 0.23 (95% confidence interval (CI) [0.13–0.33]), 0.16 (95% CI [0.07–0.25]), and 0.15 (95% CI [0.07–0.24]) standard deviations (SDs) lower than sham controls for back and neck pain, osteoarthritis, and chronic headache, respectively; the effect sizes in comparison to non-acupuncture controls were 0.55 (95% CI [0.51–0.58]), 0.57 (95% CI [0.50–0.64]), and 0.42 (95% CI [0.37–0.46]) SDs. A variety of pain severity and disability scores were used, including Visual Analog Scale (VAS) ratings, the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), and the Roland Morris Disability Questionnaire. These results were robust to a variety of sensitivity analyses, including those related to publication bias.^[9]

In the largest study of its kind to date, 454 920 patients were treated with acupuncture for headache, low-back pain, and/or osteoarthritis in an open pragmatic trial. Effectiveness was rated by the 8 727 treating physicians as marked or moderate in 76% of cases.^[10]

In a network meta-analysis comparing different

physical interventions for pain from knee osteoarthritis, acupuncture was found to be superior to sham acupuncture, muscle-strengthening exercise, *Tai Chi*, weight loss, standard care, and aerobic exercise (in ranked order). Acupuncture was found to be more effective than muscle-strengthening exercises, with a statistically significant difference = 0.49, 95% CI [0.00–0.98].^[11]

In early 2017, the American College of Physicians (ACP) published guidelines based on the evidence for the non-invasive treatment of low-back pain. For acute or subacute low-back pain, the ACP recommends non-pharmacologic treatment with acupuncture, along with superficial heat, massage, or spinal manipulation, and nonsteroidal anti-inflammatory drugs or skeletal muscle relaxants. For chronic low-back pain, the ACP also recommends acupuncture, in addition to exercise, multidisciplinary rehabilitation, mindfulness-based stress reduction, *Tai Chi*, yoga, motor control exercise, progressive relaxation, electromyography biofeedback, low-level laser therapy, operant therapy, cognitive behavioral therapy, and spinal manipulation, etc.^[12]

A systematic review and meta-analysis on acupuncture for the treatment of sciatica reported that acupuncture was superior to standard pharmaceutical care (such as ibuprofen, diclofenac, and prednisone) in reducing pain intensity (mean difference (MD) = -1.25, 95% CI [-1.63 to -0.86]) and pain threshold (MD = 1.08, 95% CI [0.98–1.17]). Effectiveness, pain intensity, and pain threshold scales were used.^[13]

A systematic review and network meta-analyses of 21 different interventions for sciatica found that acupuncture was second in global effect only to biological agents, and superior to all other interventions including non-opioid and opioid medications.^[14]

A systematic review on acupuncture and moxibustion for lateral elbow pain found moderate-level evidence that acupuncture and moxibustion were more effective than sham, and found low-level evidence that acupuncture and moxibustion may be superior or equal to standard care.^[15]

A systematic review on acupuncture for plantar heel pain found that evidence supporting the effectiveness of acupuncture was comparable to the evidence available

Box 1 Acupuncture for the Use of Numerous Conditions Including Pain Conditions: the Acupuncture Evidence Project (Mar 2013–Sept 2016)	
Evidence of positive effect	
<ul style="list-style-type: none"> ● Allergic rhinitis (perennial & seasonal) ● Chemotherapy-induced nausea and vomiting (with anti-emetics) ● Chronic low-back pain ● Headache (tension-type and chronic) ● Knee osteoarthritis ● Migraine prophylaxis ● Post-operative nausea & vomiting ● Post-operative pain 	
Evidence of potential positive effect	
<ul style="list-style-type: none"> ● Acute low-back pain ● Acute stroke ● Ambulatory anaesthesia ● Anxiety ● Aromatase inhibitor-induced arthralgia ● Asthma in adults ● Back or pelvic pain during pregnancy ● Cancer pain ● Cancer-related fatigue ● Constipation ● Craniotomy anaesthesia ● Depression (with antidepressants) ● Dry eye ● Hypertension (with medication) ● Insomnia ● Irritable bowel syndrome ● Labor pain ● Lateral elbow pain ● Menopausal hot flashes 	<ul style="list-style-type: none"> ● Modulating sensory perception thresholds ● Neck pain (some types/non-whiplash) ● Obesity ● Peri-menopausal & post-menopausal insomnia ● Plantar heel pain ● Post-stroke insomnia ● Post-stroke shoulder pain ● Post-stroke spasticity ● Post-traumatic stress disorder ● Prostatitis pain/chronic pelvic pain syndrome ● Recovery after colorectal cancer resection ● Restless leg syndrome ● Schizophrenia (with antipsychotics) ● Sciatica ● Shoulder impingement syndrome (early stage) (with exercise) ● Shoulder pain ● Smoking cessation (up to 3 months) ● Stroke rehabilitation ● Temporomandibular joint disorder



for standard care interventions such as stretching, night splints, and dexamethasone.^[16]

The use of acupuncture to relieve pain associated with surgical procedures captured the world's attention in the early 1970s. When in China, well-known *New York Times* journalist James Reston witnessed acupuncture's effectiveness on his post-operative pain. He published his personal experience with acupuncture shortly before President Richard Nixon's trip to China. Since then, reports in the scientific literature reveal that acupuncture has been used before, during, and after surgery to manage pain and to improve post-surgical recovery in a variety of contexts.^[17-25] It is noteworthy to mention that acupuncture has been reported to be effective in pain relief during and after surgical procedures on children and animals as well.^[19,20,26,27]

Nonetheless, over the past two decades in the U.S., post-operative pain management has come to rely increasingly on opioids, while underutilizing alternative analgesics such as acupuncture. In 2012, surgeons and dentists combined prescribed 16.2% of all opioids in the U.S., trailing only family practices as the leading source of opioid prescriptions at 18.2%.^[28] Eighty to ninety-four percent of patients undergoing low-risk surgical procedures fill a prescription for opioids within 7 days.^[29,30] Recent data has shown that opioid prescriptions vary widely and that the majority of surgical patients are over-prescribed opioids, as approximately 70% of pills go unused.^[31] The risk of chronic opioid use after surgery in previously non-dependent patients is determined to be 5.9%–6.5%,^[32] although in select populations such as head and neck cancer patients, the risk is up to 40%.^[33] The increase in post-operative opioid use is somewhat paradoxical considering that known adverse effects such as sedation, pneumonia,^[34,35] ileus, urinary retention, and delirium prolong patient recovery and delay the meeting of discharge goals.^[36]

Acupuncture has emerged as a promising adjunctive analgesic modality to reduce the risk of post-operative opioid dependence. A meta-analysis published in late 2017 in *JAMA Surgery* focused on non-pharmacological treatments in reducing pain after total knee arthroplasty. Thirty-nine RCTs were included in the meta-analysis (2 391 patients). Moderate-certainty level evidence showed that electrotherapy reduced the use of opioids (MD = -3.50; 95% CI [-5.90 to -1.10] morphine equivalents in milligrams per kilogram per 48 hours; $P=0.004$; $I^2=17\%$), and that acupuncture delayed opioid use (MD = 46.17; 95% CI [20.84–71.50] minutes to the first patient-controlled analgesia; $P<0.001$; $I^2=19\%$). There was low-certainty level evidence that acupuncture improved

pain (MD = 1.14; 95% CI [1.90–0.38] on a VAS at 2 days; $P=0.003$; $I^2=0\%$). Evidence showed that acupuncture out-performed cryotherapy, continuous passive motion, and preoperative exercise in the studied condition.^[37] Reduction in opioid use has been demonstrated across a wide range of both minor and major surgical procedures, including cardiac surgery,^[38] thoracic surgery,^[39] and craniotomy.^[17,40] Additionally, it was reported that acupuncture may even reduce post-operative ileus and expedite bowel recovery after colorectal cancer resection.^[41] Acupuncture is often combined with electric stimulation, and electro-acupuncture may have added clinical benefit in post-operative pain management.

A Cochrane systematic review on acupuncture or acupressure for primary dysmenorrhea found that both acupuncture and acupressure were more effective in reducing pain than placebo controls.^[42] Five other systematic reviews and/or meta-analyses on various forms of acupoint stimulation including acupuncture, acupressure, and moxibustion for primary dysmenorrhea have reported similar outcomes.^[43-47]

The effectiveness of acupuncture for labor pain is still unclear, largely due to the heterogeneity of designs and methods in studies, which have produced mixed results. While some studies reported no reduction in analgesic medications, some studies reported reduction of pain during labor, reduced use of opioid medications and epidural analgesia, and a shorter second stage of labor.^[48-50]

A systematic review of acupuncture for trigeminal neuralgia suggests that acupuncture may be equal to or superior to carbamazepine, but the evidence is weakened by the low methodological quality of some included studies.^[51]

A Cochrane systematic review on acupuncture for fibromyalgia found low- to moderate-certainty level evidence that acupuncture improves pain and stiffness compared with no treatment and standard therapy. Furthermore, electro-acupuncture is likely better than manual acupuncture for pain in fibromyalgia, although more studies with methodological rigor are warranted.^[52]

A prospective, randomized trial of acupuncture vs. morphine to treat emergency department/emergency room patients with acute onset, moderate to severe pain was conducted. Acupuncture provided more effective and faster analgesia than morphine and was better tolerated. The study included 300 patients, with 150 patients in each group. Success rate was significantly different between the 2 groups (92% in the acupuncture group vs 78% in the morphine group, $P<0.001$). Resolution time was (16 ± 8) minutes in

the acupuncture group vs (28 ± 14) minutes in the morphine group ($P < 0.005$). Overall, 89 patients (29.6%) experienced minor adverse effects; of these, 85 (56.6%) were in the morphine group and only 4 (2.6%) were in the acupuncture group ($P < 0.001$).^[53]

The above mentioned meta-analysis included 29 trials and 17 922 patients with chronic pain conditions; data on longer-term follow-up (available for 20 trials, including 6 376 patients) suggests that approximately 90% of the benefit of acupuncture relative to controls would be sustained at 12 months post-treatment. Patients can generally be reassured that treatment effects persist for some duration.^[54]

2.2 Safety and feasibility of acupuncture for pain management

Strong evidence for the safety of acupuncture in chronic pain management comes from an open pragmatic trial involving 454 920 patients who were treated for headache, low-back pain, and/or osteoarthritis. Minor adverse events were reported in 7.9% of patients while only 0.003% (13 patients) experienced severe adverse events. Minor adverse events included needling pain, hematoma, and bleeding, while serious adverse events included pneumothorax, acute hyper- or hypotensive crisis, erysipelas, asthma attack, and aggravation of suicidal thoughts.^[10] In a prospective feasibility study, acupuncture was seen as feasible, safe, and acceptable in an intensive care unit setting by patients from diverse backgrounds.^[55] A systematic review suggests that acupuncture performed by trained practitioners using clean needle technique is a generally safe procedure.^[56] The medical literature also indicates that acupuncture may be used successfully on cancer patients for symptom management due to the low risks associated with its use.^[57]

2.3 Cost-effectiveness of acupuncture for pain management

In a systematic review of 8 cost-utility and cost-effectiveness studies of acupuncture for chronic pain, the cost per quality-adjusted life-year gained was below the thresholds used by the UK National Institute for Health and Clinical Excellence for “willingness to pay.” The chronic pain conditions discussed in the systematic review included low-back pain, neck pain, dysmenorrhoea, migraine and headache, and osteoarthritis.^[58] In a cost-effectiveness analysis of non-pharmacological treatments for osteoarthritis of the knee, acupuncture was found to be the most cost-effective option when analysis was limited to high-quality studies.^[59] Using acupuncture for pain management, patients and insurers can save money and successfully manage their pain and other symptoms without the adverse risks associated

with prescription medications. A recent study from the Center for Health Information and Analysis in response to a piece of Massachusetts legislation seeking mandated coverage for acupuncture for some conditions, found that full insurance coverage for acupuncture would increase an average insured member’s monthly health insurance premium only by \$0.38 to \$0.76. Acupuncture was noted to save \$35 480, \$32 000, \$9 000, and \$4 246 per patient for migraine, angina pectoris, severe osteoarthritis, and carpal tunnel syndrome respectively.^[60] Compared to the large fees associated with imaging, prescription medications and surgery for pain conditions, acupuncture proved extremely cost-effective.

The Acupuncture Evidence Project also enumerates those conditions for which they found evidence of acupuncture being cost-effective (Box 2).^[61]

Box 2 Conditions with Demonstrated Evidence of Cost-Effectiveness	
●	Allergic rhinitis
●	Low-back pain
●	Ambulatory anaesthesia
●	Migraine
●	Chronic pain: neck pain (plus usual medical care)
●	Depression
●	Osteoarthritis
●	Dysmenorrhoea
●	Post-operative nausea and vomiting
●	Headache

A study by Da Silva^[62] published in the journal *Headache* in 2015 showed acupuncture to be at least as effective as conventional drug preventative therapy for migraine and to be safe, long lasting, and cost-effective. A 2015 study by Liodden and Norheim^[63] noted acupuncture to be potentially useful for post-operative pain and post-operative nausea and vomiting, and to be a low-cost intervention. A 2014 study by Spackman et al.^[64] showed acupuncture to be cost-effective compared to counselling or usual care alone. Two studies demonstrated acupuncture’s cost-effectiveness for the treatment of low-back pain. A study by Taylor et al.^[65] from 2014 showed that acupuncture as a complement to standard care for the relief of chronic low-back pain was highly cost-effective, costing around \$48 562 per disability-adjusted life-year (DALY) avoided. It also found that when comorbid depression was alleviated at the same rate as pain, the cost was around \$18 960 per DALY avoided. A study by Andronis et al.^[66] also identified acupuncture as likely to be cost-effective for low-back pain.



2.4 Can adjunctive acupuncture treatment reduce the use of opioid-like medications?

Some studies have reported reduced consumption of opioid-like medication (OLM) by more than 60% following surgery when acupuncture is used.^[67,68] A pilot RCT also showed a reduction by 39% in OLM use in non-malignant pain after acupuncture, an effect which lasted fewer than 8 weeks after acupuncture treatment ceased.^[69] The above mentioned meta-analysis, having moderate-certainty level evidence, showed that electro-acupuncture therapy reduced the use of opioids, and acupuncture delayed opioid use, with low-certainty level evidence indicating that acupuncture improved pain.^[37] The conclusions suggest that electro-acupuncture may be effective in reducing or delaying the use of opioid medications.

In a study examining acupuncture's effectiveness in treating pain in a military cohort of 172 at a U.S. Air Force medical center, acupuncture dramatically decreased the use of opiates and other pain medications among personnel. Opioid prescriptions decreased by 45%, muscle relaxants by 34%, non-steroidal anti-inflammatory drugs by 42%, and benzodiazepines by 14%. Quality of life measures also showed impressive changes, with some measures of improvements showing statistical significance ($P < 0.001$).^[70]

The Veterans Administration is increasingly looking to incorporate acupuncture into care, as is the U.S. Air Force and other military branches. Training of military physicians is increasing, and systems are being studied to further incorporate acupuncture. The military is rapidly incorporating this care into its offered services for service members.^[71,72]

Studies of the effects of opioid analgesia in the elderly reveal a significant burden of disease due to falls from mental impairment. This is worsened when seniors are using multiple medications affecting cognition. In a recent study, serious falls as per Medicare Part A and B ICD/CPT codes were evaluated in 5 556 nursing home residents aged 65 or greater. Seniors taking three or more central nervous system (CNS) standardized daily doses were more likely to have a serious fall than those not taking any CNS medications (adjusted odds ratio = 1.83, 95% CI [1.35–2.48]), and the authors urge, "Clinicians should be vigilant for opportunities to discontinue or decrease the doses of individual CNS medications and/or consider non-pharmacological alternatives."^[73]

A recent study in the *New Zealand Medical Journal* noted that medication-related harms were both common and created a substantial burden of disease for patients and the healthcare system. They listed opioids first among the six categories of medications causing the most significant burden.^[74] In light of the findings of these

studies and similar, utilization of non-pharmacologic treatment options such as acupuncture must be a priority of paramount status.

3 Acupuncture's analgesic mechanisms have been extensively researched and acupuncture can increase the production and release of endogenous opioids in animals and humans

Mechanisms underlying acupuncture's analgesic effects have been extensively researched for over 60 years. In animal models, acupuncture and/or electro-acupuncture has been shown to be effective for the alleviation of inflammatory, neuropathic, cancer-related, and visceral pain. Mechano-transduction of the needling stimulus at specific points on the body triggers the release of ATP and adenosine, which bind to local afferents.^[75,76] Ascending neural pathways involving A β , A δ , and C sensory fibres have been mapped (using techniques such as single fiber recordings with Evans blue dye extravasation), as have been a mesolimbic analgesic loop in the brain and brainstem, descending pathway mechanisms, dopaminergic contributors, and cytokine, glutamate, nitric oxide, and gamma-amino butyric acid (GABA) effects. Acupuncture analgesia has been shown to involve several classes of opioid neuropeptides including enkephalins, endorphins, dynorphins, endomorphins, and nociceptin (also known as orphanin FQ). Among the non-opioid neuropeptides, substance P, vasoactive intestinal peptide, and calcitonin gene-related peptide have been investigated for their roles in both the analgesic and anti-inflammatory effects of acupuncture.^[77–80]

Given that acupuncture analgesia activates the production and release of endogenous opioids and activates μ and δ opioid receptors, it is feasible that acupuncture, used in conjunction with OLM, might alleviate pain with a lower OLM dose for patients already taking OLM.^[81] This idea is further supported by evidence that acupuncture increases μ opioid receptor binding potential, allowing for effective analgesia at lower doses of OLM.^[82] For patients not yet prescribed OLM, acupuncture should be recommended prior to OLM prescription commencing. This would be in-line with existing guidelines, such as those by the ACP^[12] and the CDC,^[83] which recommend that safe and effective non-opioid alternatives should first be exhausted before resorting to OLM.

It is important to note as well that opioids as a monotherapy are often not as successful as may be thought in the general public perception. A recent systematic review of opioid analgesics for low-back pain, which included 7 925 participants, found

that opioids were poorly tolerated and for those who tolerate them the effect is unlikely to be clinically important within guideline recommended doses.^[84] The first ever RCT evaluating the long-term effectiveness of opioids, found that those on long-term opioid analgesia were actually in marginally more pain at 12 months than those in the non-opioid group.^[85] Hence, complementary methods of pain control are critical to successful patient management.

4 Acupuncture is effective for the treatment of chronic pain involving maladaptive neuroplasticity

Adverse neuroplastic changes can present a challenge in pain management, as maladaptive neuroplasticity can be associated with severe chronic pain that is resistant to treatment. Via peripheral stimulation, acupuncture may relieve the symptoms of patients affected by problematic neuroplastic changes. There is evidence that acupuncture has the capacity to reverse adverse neuroplastic changes in the dorsal horns of the spine, as well as in the somatosensory cortex.^[86-89] This suggests that acupuncture may have an important role in treating chronic pain which involves adverse neuroplastic changes.

5 Acupuncture is a very promising, already utilized adjunctive therapy in opiate dependency and rehabilitation

In 1973, Wen et al.^[90] from Hong Kong published an accidental finding that ear acupuncture treatment for respiratory patients had apparently alleviated opioid withdrawal signs and symptoms. These findings were replicated by others around the world, including in New York and Sydney in the mid-1970s. In 1985, Dr. Michael Smith and colleagues in New York established the National Acupuncture Detoxification Association (NADA), which today operates in over 40 countries with an estimated 25 000 providers. There are more than 1 000 programs in the U.S. and Canada that now use acupuncture to help addicts overcome their addictions.^[91]

Evidence for acupuncture's place in addiction treatment has been found in both animal and human studies. In 2009, Hu et al.^[92] found that electro-acupuncture in rats appeared to affect dopamine neurons in the ventral tegmental area, meaningfully improving the deleterious effects caused to this area by opioid medication. In 2012 Lee et al.^[93] demonstrated that electro-acupuncture could be used to decrease drug-seeking behaviour in rats. As far back as 1978 it was demonstrated that acupuncture decreased biochemical markers of stress in heroin

addicts compared to observational controls.^[94] In 2014 Chan et al.^[95] demonstrated that acupuncture decreased the amount of morphine used by addicts in treatment, and simultaneously improved sleep in the treatment subjects. Acupuncture for addiction is a versatile modality that can be effortlessly integrated into many environments including prisons, in- and outpatient programs, community centers, disaster relief, and humanitarian aid efforts. Furthermore, acupuncture addiction protocols can address acute and prolonged withdrawal symptoms, stress and anxiety related to drug withdrawal, and help prevent relapse. Using drugs to treat those already drug-addicted is not a rational plan of action, and finding sound, non-pharmacologic treatment options is of paramount importance.

A meta-analysis done in 2012 concluded that “the majority [of studies] agreed on the efficacy of acupuncture as a strategy for the treatment of opiate addiction” and that “neurochemical and behavioral evidence has shown that acupuncture helps reduce the effects of positive and negative reinforcement involved in opiate addiction by modulating mesolimbic dopamine neurons. Moreover, several brain neurotransmitter systems involving opioids and GABA have been implicated in the modulation of dopamine release by acupuncture.”^[96] In a recent RCT involving 28 newborns with neonatal abstinence syndrome, laser acupuncture plus OLM significantly reduced the duration of oral morphine therapy when compared to OLM alone.^[97] The mechanism for acupuncture in opiate withdrawal was found to be mediated by the endogenous opioid “dynorphin” binding to κ opioid receptors.^[98] While considerable research on acupuncture's role in addiction is still greatly needed, long-standing and new data provide a sound foundation for that future research. Demonstration of trans-species effects with multiple, plausible mechanisms and documented clinical efficacy in humans for opioid addiction specifically, coupled with vast, existing clinical precedent of use in this realm, argues strongly for acupuncture's likely value in this domain.

6 Acupuncture has been recommended as a first line, non-pharmacologic therapy by the FDA as well as the NASEM in coping with the opioid crisis; the Joint Commission has also mandated that hospitals provide non-pharmacologic pain treatment modalities

The U.S. FDA released proposed changes to its opioid prescription guidelines in early May 2017. Entitled a “Blueprint for Prescriber Education for Extended-Release and Long-Acting Opioids,” the



guidelines now recommend that doctors become informed about non-pharmacologic options for pain control to help avoid the overuse of opioids.^[5] Per the FDA's request, the NASEM released a report to outline the state of the science regarding prescription opioid abuse and misuse, as well as the evolving role that opioids play in pain management. The new NASEM report on pain management and opioids recommends more public education, reimbursement models, and support for non-drug approaches to pain treatment. It systematically summarizes the evidence for acupuncture's clinical benefits in treating different pain conditions, and provides an overview of some of the basic science underlying acupuncture's mechanisms in pain management.^[6] Further, effective January 1, 2018, the Joint Commission has mandated that hospitals provide non-pharmacologic pain treatment modalities.^[7] Acupuncture is ideally suited to fulfil this mandate. These official, evidence-based clinical guidelines are in line with global healthcare trends. As of November 2015, acupuncture had over 870 recommendations in official clinical guidelines for over 100 conditions from institutions in over 30 countries.^[99]

7 Among the most commonly recommended, non-pharmacological management options for pain relief, evidence supports acupuncture as the most specific and effective for opioid abuse and overuse

Several forms of non-pharmacological management options for acute and chronic pain have been examined, including physical therapy, spinal column manipulation, yoga, *Tai Chi*, cognitive behavioral therapy, as well as others. Among those therapies commonly recommended by medical authorities, evidence supports acupuncture as the most specific in targeting the endogenous opioid system. There is more evidence that acupuncture can induce endorphins to cope with acute and chronic pain in basic research than for any other non-pharmacological approach for pain.^[12,37,53,60] Other mechanisms for acupuncture's effects have also been discussed above.

8 Acupuncture is widely available from qualified practitioners nationally

In 2013 more than 28 000 licensed acupuncturists were estimated to be practicing in the U.S., with many more in training.^[100] A 2015 study found the number of professionals practicing as "Licensed Acupuncturists" (or state equivalent) to be approximately 34 400. The number of licensed acupuncturists was noted to have

increased by 23.3% and 52.1% compared to the years 2009 ($n = 27\ 965$) and 2004 ($n = 22\ 671$) respectively, increasing about 1 266 per year.^[101] Currently, the Council of Colleges of Acupuncture and Oriental Medicine has 57 schools in its membership,^[102] with approximately ten schools offering doctoral degrees. The National Certification Council for Acupuncture and Oriental Medicine has certified more than 18 000 practitioners for minimal competency.^[103] The practitioners emerging from this educational and testing infrastructure are the most highly trained in Chinese medicine as a complete system, and the training capacity is vastly underutilized. This system could produce many more practitioners were demand increased. The American Academy of Medical Acupuncture also represents more than 1 300 medical doctors trained to offer acupuncture services, and has approved nine programs for medical doctor certification in acupuncture.^[104] One certification program alone has trained more than 6 000 physicians in medical acupuncture,^[105] so a conservative estimate of the total number of physicians trained would be approximately 10 000, though the number actively practicing acupuncture is unknown. Most states allow physicians to practice acupuncture, with some specifying additional training.^[106] Increased coverage and demand for acupuncture will lead to a greater supply of providers as well. As noted above, NADA providers are estimated at 25 000 individuals, with more than 1 000 programs in the U.S. and Canada.

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10 Competing interests

The authors declare that they have no competing interests. Comments or corrections are welcomed and appreciated.

Appendix 1 Effectiveness of Acupuncture (to be continued)

Author, year	Topic/intervention	Participants/population	Primary outcomes	Key findings	Study quality
Vickers et al., 2012 ^[9]	Acupuncture versus sham acupuncture and non-acupuncture in back, neck and shoulder pain, chronic headache, and osteoarthritis	Systematic review of 31 RCTs (17 922 subjects) and meta-analysis of individual patient data from 29 of these 31 RCTs in back, neck and shoulder pain; chronic headache; osteoarthritis	A variety of pain severity and disability scores such as VAS, WOMAC, Roland Morris Disability Questionnaire	Acupuncture was superior to sham acupuncture and non-acupuncture for each pain condition	High-quality evidence
Weidenhammer et al., 2007 ^[10]	Acupuncture for headache, low-back pain, and osteoarthritis	Open pragmatic trial of 454 920 subjects with headache, low-back pain, and osteoarthritis	Treating physician rating of “marked, moderate, minimal or poor improvement (which included no improvement and worse)”	Physician ratings: 22% marked, 54% moderate, 16% minimal and 4% poor improvement	Low-quality evidence—open pragmatic trial with no blinding and no external assessors
Corbett et al., 2013 ^[11]	Comparison of 22 physical therapies for knee osteoarthritis pain	Review of 152 trials and network meta-analysis of 12 RCTs with low risk of bias comparing 22 physical therapies in knee osteoarthritis pain	Knee pain	Acupuncture was equal to balneotherapy and superior to sham acupuncture, muscle-strengthening exercise, <i>Tai Chi</i> , weight loss, standard care and aerobic exercise (in ranked order)	110 of 152 studies analysed were of poor quality. Network meta-analysis included 12 RCTs with low risk of bias
Ji et al., 2015 ^[13]	Acupuncture versus standard pharmaceutical care in sciatica	Systematic review and meta-analysis of 12 RCTs in sciatica	Effectiveness, pain intensity, and pain threshold	Acupuncture was superior to standard pharmaceutical care in effectiveness, reducing pain intensity and pain threshold	Low- to moderate-quality evidence
Lewis et al., 2015 ^[14]	Comparison of 21 different interventions for sciatica	Systematic review and network meta-analyses of 122 studies including 90 randomized or quasi-randomized controlled trials comparing 21 different interventions for sciatica	Global effect, and pain intensity	In global effect and reduction in pain intensity, acupuncture was second only to biological agents (cytokine-modulating drugs), and superior to all other interventions tested including non-opioid and opioid medications	9% of studies had a strong overall quality rating; 7% of studies had a strong overall external validity rating; 21% of studies used both adequate randomization and adequate or partially adequate allocation concealment

Appendix 1 Effectiveness of Acupuncture (continuation 1)

Author, year	Topic/intervention	Participants/population	Primary outcomes	Key findings	Study quality
Gadau et al., 2014 ^[15]	Acupuncture and/or moxibustion versus sham acupuncture, another form of acupuncture, or conventional treatment in lateral elbow pain	Systematic review of 19 RCTs	Pain, and grip strength	Acupuncture is more effective than sham acupuncture (moderate-quality studies); acupuncture or moxibustion is more effective than conventional treatment (low-quality studies)	Low- to moderate-quality evidence
Cho et al., 2015 ^[20]	Real versus sham acupuncture in acute post-operative pain after back surgery	Systematic review and meta-analysis of 5 trials	24-hour post-operative pain intensity on VAS; 24-hour opiate demands	Real acupuncture was superior to sham in reducing pain intensity but not opiate demand at 24 hours	3 of 5 trials were high quality
Levett et al., 2014 ^[48]	Acupuncture, standard care, sham acupuncture, acupressure and mixed controls in various combinations in labor pain	A critical narrative review of 4 systematic reviews in labor pain	Pain intensity, analgesic use, and length of labor	Acupuncture reduces pain intensity, analgesic use and length of labor	Conflicting evidence
Clark et al., 2012 ^[16]	Acupuncture versus various comparators including standard care, sham acupuncture and other forms of acupuncture in plantar heel pain	Systematic review of 5 RCTs and 3 non-randomized comparative trials	Various pain and disability scales (morning pain, walking pain, and tenderness)	Acupuncture for plantar heel pain is supported by evidence which is equivalent to evidence supporting standard care (stretching, splints, and dexamethasone)	Evidence at levels I and II supporting the effectiveness of acupuncture for heel pain, leading to a recommendation at Grade B
Deare et al., 2013 ^[52]	Manual and electro-acupuncture compared with sham acupuncture, standard therapy and no treatment in fibromyalgia	Cochrane systematic review of 9 RCTs in fibromyalgia	Pain, stiffness, sleep, fatigue and global wellbeing	Acupuncture improves pain and stiffness compared to standard therapy and no treatment, but not compared to sham acupuncture	Low- to moderate-quality evidence
Smith et al., 2011 ^[42]	Acupuncture or acupressure versus placebo control, usual care or pharmacological treatment in primary dysmenorrhea	Cochrane systematic review of 10 RCTs (944 subjects) on acupuncture (6) or acupressure (4) for primary dysmenorrhea	Pain relief, analgesic use, quality of life, improvement in menstrual symptoms, and absenteeism	Acupuncture was superior to placebo and Chinese herbs in pain relief, and superior to medication and Chinese herbs in reducing menstrual symptoms. Acupressure was superior to placebo in pain relief and reducing menstrual symptoms	Low risk of bias in 50% of included RCTs

Appendix 1 Effectiveness of Acupuncture (continuation 2)

Author, year	Topic/intervention	Participants/population	Primary outcomes	Key findings	Study quality
Abaraogu et al., 2015 ⁽⁴³⁾	Acupuncture or acupressure versus placebo control, wait list or pharmacological treatment in primary dysmenorrhea	Systematic review of 8 RCTs (> 3 000 subjects) and meta-analysis of 4 RCTs	Pain intensity (VAS, McGill scale), quality of life, and blood nitric oxide	Acupuncture and acupressure reduced pain, while acupuncture also improved quality of life	Moderate-quality evidence
Chen et al., 2013 ⁽⁴⁷⁾	Acupuncture or acupressure at acupoint SP6 versus minimal stimulation at SP6 or stimulation of another point in primary dysmenorrhea	Meta-analysis of acupuncture (3) and acupressure (4) RCTs in primary dysmenorrhea	Pain intensity (VAS)	Acupuncture is effective and acupressure may be effective at SP6 for pain relief	Acupuncture trials had low to moderate risk of bias; acupressure trials had high risk of bias
Cho et al., 2010 ⁽⁴⁴⁾	Acupuncture versus sham acupuncture, pharmacological treatment or Chinese herbs in primary dysmenorrhea	Systematic review of 27 RCTs in primary dysmenorrhea	Pain intensity (VAS, Menstrual Pain Reduction Score, and other pain scores)	Acupuncture was superior to pharmacological treatment or Chinese herbs in pain relief	Only 5 out of 27 trials had low risk of bias
Chung et al., 2012 ⁽⁴⁶⁾	Acupoint stimulation versus non-acupoint stimulation or medication in primary dysmenorrhea	Systematic review of 30 RCTs (> 3 000 subjects) and meta-analysis of 25 RCTs	Pain intensity, and plasma prostaglandin F2/ prostaglandin E2 ratio	Acupoint stimulation was superior in short-term pain relief to stimulation on non-acupoints. Non-invasive stimulation of acupoints was more effective than invasive stimulation	Some trials were of low quality
Xu et al., 2014 ⁽⁴⁵⁾	Various forms of acupoint stimulation (including acupuncture, moxibustion and other methods) versus a variety of controls in primary dysmenorrhea	Meta-analysis of 20 RCTs (2 134 subjects) of acupoint stimulation for primary dysmenorrhea	Pain relief	Acupoint stimulation was more effective than controls for pain relief	Low- to moderate-quality evidence

RCT: randomized controlled trial; VAS: Visual Analog Scale; WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index. There is currently debate within the scientific and academic communities on how to perform high-quality studies on acupuncture. It is widely recognized that standards applied to drug trials are inappropriate for acupuncture studies, as it is impossible to effectively blind patients to treatment with acupuncture as can be done with medications. Hence, this literature review, adhering to standards for drug studies, may undervalue some existing studies, and hence the strength of acupuncture for care may also be underestimated.



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