

Acupuncture for chronic pain and depression in primary care: a programme of research

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Scientific summary

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Background

Acupuncture is widely practised in the UK, with an estimated 4 million treatments provided a year, primarily for chronic pain conditions such as musculoskeletal pain and headache or migraine. In addition to chronic pain conditions, psychological distress, including depression, has been a common reason that people have consulted acupuncturists. The evidence base on acupuncture has been patchy, with some controversy regarding the clinical benefits and specifically the extent that acupuncture is more than simply a placebo. Clinical questions remain as to the effect of acupuncture in everyday practice and there are unanswered questions regarding whether or not acupuncture is cost-effective. One of the challenges in the field has been the quality of the available evidence. For most conditions, systematic reviews of acupuncture have had a limited ability to draw any definitive conclusions regarding effectiveness. As with research into many other physical therapies for chronic pain, there have been too many underpowered trials conducted and the methodological standards have been insufficiently robust. In this climate of uncertainty, however, there has been a recent and dramatic increase in the quality and quantity of trials of acupuncture, especially for chronic pain conditions, which has provided this programme of research a unique opportunity to substantially reduce the uncertainty. In this context, our primary aim was to use high-quality methods and the best evidence available to determine the clinical and economic impact of acupuncture for chronic pain and depression.

Acupuncture for chronic pain

Although acupuncture is widely used for chronic pain, there is limited understanding of how it works, which in turn fuels some of the uncertainty as to its potential role as a treatment modality. The uncertainty is associated with a concern that acupuncture might simply be a theatrical placebo and the suggestion that when issues of bias are taken into account, the size of any effect might vanish. To address the uncertainty, in our first study we set out to determine the effect size of acupuncture for chronic pain, whether acupuncture is compared with sham acupuncture or with a non-acupuncture control, based on direct trial data on these comparisons. On building a collaboration of key triallists, the Acupuncture Triallists' Collaboration (ATC), we were able to conduct an individual patient data (IPD) meta-analysis. To establish eligible studies we identified randomised controlled trials (RCTs) of acupuncture for the four chronic pain conditions in which allocation concealment was determined unambiguously to be adequate. Data from 29 of 31 eligible RCTs, with a total of 17,922 patients, were analysed. Our primary result, when including all eligible RCTs, was that acupuncture was statistically significantly more effective than both sham controls and non-acupuncture controls for all four pain conditions ($p < 0.001$). When an outlying set of RCTs that strongly favoured acupuncture was excluded, the effect size across each pain condition was similar. Patients receiving acupuncture had less pain than those receiving sham controls, with effect sizes based on standardised mean differences (SMDs) of 0.23 [95% confidence interval (CI) 0.13 to 0.33], 0.16 (95% CI 0.07 to 0.25) and 0.15 (95% CI 0.07 to 0.24) for back and neck pain, osteoarthritis and chronic headache, respectively. In the comparison between acupuncture and non-acupuncture controls, effect sizes were 0.55 (95% CI 0.51 to 0.58), 0.57 (95% CI 0.50 to 0.64) and 0.42 (95% CI 0.37 to 0.46), respectively. A variety of sensitivity analyses was conducted, including those related to publication bias, with little impact on the main findings of the study. To conclude, in these high-quality studies, a clinically relevant and statistically significant difference was found between acupuncture and non-acupuncture controls, suggesting that acupuncture is a suitable referral option for chronic pain. Statistically significant differences between true and sham acupuncture indicate that acupuncture is more than a placebo.

Physical therapies for osteoarthritis

Many systematic reviews have evaluated individual types of physical treatments for osteoarthritis of the knee, but no study has compared these different physical treatments against each other in the same analysis. In a second study we used a network meta-analysis to address the question of how effective physical treatments for osteoarthritis of the knee are, when compared with each other, for relieving pain. We reviewed the literature up to January 2013, which involved searching 17 electronic databases. We identified RCTs of physical treatments in patients with osteoarthritis of the knee in which pain was reported as an outcome. In a network meta-analysis, both direct and indirect evidence was synthesised to compare the effectiveness of acupuncture with that of other relevant physical treatments for alleviating pain. In total, 114 trials (covering 22 treatments and 9709 patients) were included in the analysis. Many trials were classed as being of poor quality with a high risk of bias in several domains. Eight interventions statistically significantly outperformed standard (usual) care, producing an improvement in pain compared with standard care: interferential therapy, acupuncture, transcutaneous electrical nerve stimulation (TENS), pulsed electrical stimulation, balneotherapy, aerobic exercise, sham acupuncture and muscle-strengthening exercise. The better-quality studies, most commonly of acupuncture (11 trials), muscle-strengthening exercise (nine trials) and sham acupuncture (eight trials), were included in a sensitivity analysis. Acupuncture was statistically significantly more effective than muscle-strengthening exercise and sham acupuncture (SMD 0.49, 95% CI 0.00 to 0.98; and 0.34, 95% CI 0.03 to 0.66, respectively). Acupuncture was also statistically significantly better than standard care (SMD 1.01, 95% CI 0.61 to 1.43). To conclude, in a network meta-analysis, acupuncture was found to be one of the more effective physical treatments for alleviating osteoarthritis knee pain in the short term. However, given that much of the evidence was of poor quality, there is uncertainty about the effectiveness of many physical treatments.

Towards evaluating the cost-effectiveness of acupuncture for osteoarthritis

To address the question of the cost-effectiveness of acupuncture for chronic pain, we have benefited from the availability of the data from the ATC repository. In this third study we conducted a network meta-analysis of the individual patient-level data from the ATC repository. By synthesising all of the data, including indirect data, we derived treatment effect estimates, a key parameter for cost-effectiveness analyses to be used for resource allocation decisions. In this primarily methodological study, new Bayesian methods for analysing multiple individual patient-level data sets reporting heterogeneous continuous outcomes were developed. An essential step towards a cost-effectiveness analysis is a preference-based measure of health-related quality of life, such as the EuroQol-5 Dimensions (EQ-5D). To synthesise heterogeneous outcomes, we used mapping to convert and compare heterogeneous outcomes on to the EQ-5D summary index scale. The models developed entailed a Bayesian random-effects network meta-analysis specification, including exchangeable pain type interaction effects. The implications for cost-effectiveness analysis were also demonstrated. The methods were illustrated using a case study of acupuncture for chronic pain in primary care, including headache/migraine, musculoskeletal pain and osteoarthritis of the knee. By using the same evidence base as in the first study, our analysis included approximately 17,500 patients from 28 trials (we were unable to use IPD from one trial), in which we compared acupuncture, sham acupuncture and usual care with each other. The synthesis of mapped EQ-5D estimates found that acupuncture was effective compared with usual care, with median treatment effects estimated as 0.056 [95% credible interval (CrI) 0.021 to 0.092] for headache/migraine, 0.082 (95% CrI 0.047 to 0.116) for musculoskeletal pain and 0.079 (95% CrI 0.042 to 0.114) for osteoarthritis of the knee. The EQ-5D benefit of acupuncture over sham acupuncture was smaller and more uncertain (headache: 0.004, 95% CrI -0.035 to 0.042; musculoskeletal pain: 0.023, 95% CrI -0.007 to 0.053; osteoarthritis of the knee: 0.022, 95% CrI -0.014 to 0.060). Although not all relevant interventions were compared for decision-making purposes, cost-effectiveness results suggest that when acupuncture is compared with usual care alone it is cost-effective, with incremental cost-effectiveness ratios (ICERs) ranging from £7000 to £14,000 per quality-adjusted life-year (QALY) across the pain types of headache/migraine, musculoskeletal

pain and osteoarthritis of the knee. In this methodologically oriented case study we showed that the mapping of heterogeneous outcomes on to the EQ-5D summary index provides a useful step towards conducting a cost-effectiveness analysis.

Cost-effectiveness of non-pharmacological treatments for osteoarthritis

In a fourth study within this programme of research, we conducted an economic evaluation to evaluate the cost-effectiveness of non-pharmacological treatments used to reduce chronic pain in osteoarthritis of the knee. We used novel network meta-analysis methods to synthesise RCT evidence for 17 active interventions and three control interventions. Data were obtained from the systematic review carried out in the second study, which were available for 88 RCTs including 7507 patients. IPD from the first study were available for five of the RCTs, including 1329 patients. A wide range of health-related quality-of-life outcomes were reported in the trials. As the ultimate objective of the analysis was to inform resource allocation decisions in the UK, data from these instruments were mapped to EQ-5D preference weights prior to synthesis, extending methods developed in the third study. Sensitivity analyses were conducted to address potential bias associated with poor study conduct and to explore the importance of the time point of reporting for the study results. Resource use associated with the interventions was estimated from trial data, expert opinion, the literature and information obtained from NHS trust websites. Non-intervention resource use related to changes in EQ-5D was obtained from another UK trial. Outcomes and costs were synthesised using an area-under-the-curve cost-effectiveness model with a time horizon of 8 weeks. When all trials were included in the synthesis, TENS was cost-effective with an ICER of £2690 per QALY compared with usual care. When the analysis was restricted to trials with adequate allocation concealment, acupuncture was cost-effective with an ICER of £13,502 per QALY compared with TENS. There were limited data regarding the long-term effects of many non-pharmacological interventions used to treat osteoarthritis of the knee. The active and control interventions in the trials informing this analysis were subject to heterogeneity in the method, duration and intensity with which they were administered. These results are subject to some decision uncertainty and the expected value of perfect information is relatively high, suggesting that additional research may be cost-effective.

Acupuncture or counselling for depression

Depression is a significant cause of morbidity. Many patients have communicated an interest in non-pharmacological therapies to their general practitioners. Systematic reviews of acupuncture and counselling for depression in primary care have identified limited evidence. The aim of the fifth study was to evaluate acupuncture compared with usual care and counselling compared with usual care for patients who continue to experience depression in primary care. Moreover, a cost-effectiveness analysis is needed to understand whether or not such therapies should be considered a good use of limited health resources. In total, 755 patients with depression (Beck Depression Inventory-II score of ≥ 20) were recruited to a RCT carried out in 27 primary care practices in the north of England. Allocation was to one of three arms using a ratio of 2 : 2 : 1 to acupuncture ($n = 302$), counselling ($n = 302$) and usual care alone ($n = 151$). The difference in mean Patient Health Questionnaire-9 items (PHQ-9) score at 3 months was the primary outcome. Patients were followed up over 12 months and analysis was by intention to treat. Additional quantitative and qualitative substudies were conducted. Data on PHQ-9 scores were available for 614 patients at 3 months and 572 patients at 12 months. A mean of 10 sessions was attended for acupuncture and a mean of nine sessions was attended for counselling. There was a statistically significant reduction in mean PHQ-9 depression score at 3 months for acupuncture compared with usual care (-2.46 , 95% CI -3.72 to -1.21) and counselling compared with usual care (-1.73 , 95% CI -3.00 to -0.45), and at 12 months for acupuncture (-1.55 , 95% CI -2.41 to -0.70) and counselling (-1.50 , 95% CI -2.43 to -0.58) compared with usual care. When controlling for time and attention, no significant differences in clinical outcome were found between acupuncture and counselling. No serious treatment-related adverse events were reported. The trial was not designed to separate

out specific from non-specific effects. Acupuncture and counselling were found to have higher mean QALYs and costs than usual care. In the base-case analysis, acupuncture had an ICER of £4560 per additional QALY and was cost-effective with a probability of 0.62 at a cost-effectiveness threshold of £20,000 per QALY. A scenario analysis of counselling compared with usual care, excluding acupuncture as a comparator when inappropriate or unavailable, resulted in an ICER of £7935 and a probability of being cost-effective of 0.91. To summarise, patients with ongoing depression in primary care who received a short course of either acupuncture or counselling experienced statistically significant reductions in depression compared with usual care alone.

Conclusion

In conclusion, this programme of research has provided the most substantive evidence to date on acupuncture and its potential impact. Drawing on the existing data from RCTs, we used an IPD meta-analysis and found acupuncture to be clinically effective across the chronic pain conditions of headache and migraine, back and neck pain, and osteoarthritis of the knee. Our evidence from this data set suggests that acupuncture is a statistically significantly more effective intervention than placebo. In a network meta-analysis, our evidence across a range of physical therapies for osteoarthritis of the knee suggested that acupuncture is associated with more high-quality trials than any of the other therapies and is also one of the most effective therapies. Acupuncture was also cost-effective if only high-quality trials were analysed. When all trials were included in the synthesis, including both low- and high-quality trials, we found TENS to be cost-effective. In the trial that we conducted on depression, we found that acupuncture and counselling were statistically significantly better than usual care and that acupuncture was also cost-effective.

There remains some uncertainty regarding our results. For example, with regard to the cost-effectiveness analyses of acupuncture for musculoskeletal pain and headache and migraine, not all competing therapies relevant to decision-making were included in the analysis. There are few data regarding the long-term effects of many non-pharmacological interventions used to treat osteoarthritis of the knee, and sensitivity analyses suggested that the cost-effectiveness model results may be sensitive to the magnitude of these effects. When comparing acupuncture with usual care for depression, there was no control for non-specific effects, although we did control for time and attention when comparing acupuncture with counselling. Nevertheless, our programme of research has used high-quality methods to provide the best possible data on the clinical effectiveness and cost-effectiveness of acupuncture for chronic pain and depression. Robust evidence is in the interests of all stakeholders and our results will be used to inform patients, practitioners, policy-makers and commissioners of services.

Trial registration

The trial of acupuncture and counselling for depression is registered as ISRCTN63787732.

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