Research Paper

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The persistence of the effects of acupuncture after a course of treatment: a meta-analysis of patients with chronic pain

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Abstract

There is uncertainty regarding how long the effects of acupuncture treatment persist after a course of treatment. We aimed to determine the trajectory of pain scores over time after acupuncture, using a large individual patient data set from high-quality randomized trials of acupuncture for chronic pain. The available individual patient data set included 29 trials and 17,922 patients. The chronic pain conditions included musculoskeletal pain (low back, neck, and shoulder), osteoarthritis of the knee, and headache/migraine. We used meta-analytic techniques to determine the trajectory of posttreatment pain scores. Data on longer term follow-up were available for 20 trials, including 6376 patients. In trials comparing acupuncture to no acupuncture control (wait-list, usual care, etc), effect sizes diminished by a nonsignificant 0.011 SD per 3 months (95% confidence interval: −0.014 to 0.037, $P = 0.4$) after treatment ended. The central estimate suggests that approximately 90% of the benefit of acupuncture relative to controls would be sustained at 12 months. For trials comparing acupuncture to sham, we observed a reduction in effect size of 0.025 SD per 3 months (95% confidence interval: 0.000-0.050, $P = 0.050$), suggesting approximately a 50% diminution at 12 months. The effects of a course of acupuncture treatment for patients with chronic pain do not seem to decrease importantly over 12 months. Patients can generally be reassured that treatment effects persist. Studies of the cost-effectiveness of acupuncture should take our findings into account when considering the time horizon of acupuncture effects. Further research should measure longer term outcomes of acupuncture.

Keywords: Acupuncture, Chronic pain, Meta-analysis, Trajectory

1. Introduction

In an individual patient data meta-analysis of nearly 18,000 patients on high-quality randomized trials involving patients with chronic pain, the Acupuncture Trialists' Collaboration reported that acupuncture provided small but statistically significant benefits over sham (placebo) acupuncture, a result that can be distinguished from bias.[35] Moreover, a robust and larger effect size was observed when acupuncture was compared with no acupuncture control, with the difference being clinically relevant.[35] The data from each trial entered into the collaboration meta-analysis were the outcomes at the trial's primary endpoint. For instance, if a trial measured outcome after 12 weeks of treatment and then 3 months later, but the authors specified the posttreatment follow-up as primary, then it would be the 12-week follow-up used in the meta-analysis.

For approximately two-thirds of the trials in the meta-analysis, the primary endpoint was between 1 and 3 months after the end of treatment. The primary endpoint was 1 year or more after randomization for only 3 trials. This is problematic in the context of chronic pain. For a patient who has endured chronic pain for a decade or more, the promise of a few months relief, while welcome, is less relevant than the question of whether an intervention provides benefits over the longer term. The duration of acupuncture effects also has clear health economic implications. Whether the benefits of a course of acupuncture treatment are worth its cost depends critically on how long those benefits last.

In this article, we analyze individual patient data from the Acupuncture Trialists' Collaboration to determine the time course of acupuncture effects. We sought to take advantage of the fact that many of the eligible trials measured outcome at more than one time point after the end of treatment. By comparing how differences between groups change between 2 posttreatment time points, we aimed to estimate the degree to which the effects of acupuncture persist.

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2. Methods

2.1. Systematic review

Trials included in these analyses were identified through a systematic literature review that has been previously described.[35,36] The search included trials of acupuncture for chronic pain where allocation concealment was determined unambiguously to be adequate. Eligible pain patients were those with nonspecific low back or neck pain, shoulder pain, chronic headache/migraine, or osteoarthritis. This search resulted in the identification of 31 trials and individual patient data were obtained from 29 trials. Of these, 18 trials compared acupuncture with no acupuncture controls (**Table 1**). Control groups included no treatment, wait-list, rescue medication, usual care, or protocol-guided care. Patients who were allocated to a wait-list were offered treatment at the end of the trial period. A further 20 trials compared acupuncture with sham acupuncture (**Table 2**). Nine of these trials had 3 arms, with patients allocated to acupuncture, no acupuncture, or a sham control. We have previously explored the impact of the choice of control group on the effect size of acupuncture, which showed that the more active the control the smaller the apparent effect of acupuncture.[24]

2.2. Outcome

The primary outcome used for this analysis was pain as defined by the study authors. Where multiple criteria were considered in the primary outcome (eg, a response defined as either a 33% reduction in pain or a 50% reduction in pain medication) or if the primary outcome was inherently categorical, we instead used a continuous measure of pain. To make outcome measurements comparable between different trials, all pain measurements were standardized by dividing by pooled SD and multiplied by 100. Because higher pain scores correspond to lower levels of pain, a positive pain change score corresponds to an improvement (less pain) from baseline, ie, if a patient had a score of 100 at baseline and 50 after treatment, then they were actually in more pain, not less pain.

2.3. Analysis

For a trial to be included in this meta-analysis, the primary outcome must have been measured at least twice after the end of treatment. For trials in which control group patients were later offered acupuncture treatment, data from both acupuncture and control patients were dropped from all time points after the time at which control patients began receiving treatment. Trials were excluded if they had only one measurement after the end of treatment, if all outcome measurements were only during treatment, or if the primary outcome was measured only after control patients began to receive acupuncture. In this analysis, we used all time points in a trial, not just the time point specified as primary by the study authors.

In the primary analysis,[35] we did not find evidence that the effects of acupuncture differed by indication. Hence, we planned to include all trials together and then examine the data to determine whether there was evidence of a difference in time course by indication, a "lump then split" approach.

To estimate the time course of acupuncture effects, we used the *xtgee* command in Stata to create a longitudinal model taking into account the correlation between an individual patient's scores over time. We used the pain intensity score as the dependent variable with baseline score, time, and treatment group and an interaction term for group and time as predictors. Because the length of acupuncture treatment varied between trials, time was defined as the number of days since the end of treatment for this model.

Table 1

Trials with a no acupuncture control.

Trial name	Pain condition	Control patients offered acupuncture treatment (crossover)	Average length of treatment, wk	Time points after end of treatment	Included in meta-analysis
Foster et al.[10]	Osteoarthritis	No	3	Weeks 3, 23, and 49	Yes
Linde et al.[22]	Migraine	At 12 wk	8	Week 4	No
Melchart et al.[25]	Headache	At 12 wk	8	Week 4	No
Thomas et al.[30]	Low back pain	No	12	Weeks 1, 40, and 92	Yes
Salter et al.[26]	Neck	No	12	Week 1	No
Berman et al.[3]	Osteoarthritis	No	26	End of treatment	No
Cherkin et al.[6]	Low back pain	No	10	End of treatment and week 42	Yes
Diener et al.[8]	Migraine	No	6	End of treatment and weeks 7 and 20	Yes
Scharf et al.[27]	Osteoarthritis	No	6	Weeks 7 and 20	Yes
Haake et al.[15]	Low back pain	No	6	End of treatment and weeks 7 and 20	Yes
Vickers et al.[37]	Headache	No	6	Weeks 1 and 40	Yes
Williamson et al.[39]	Osteoarthritis	No	6	Weeks 1 and 6	Yes
Witt et al.[40]	Osteoarthritis	At 8 wk	8	End of treatment	No
Witt et al.[41]	Neck	At 12 wk	12	All measurements after crossover	No
Witt et al.[42]	Osteoarthritis	At 12 wk	12	All measurements after crossover	No
Jena et al.[17]	Headache	At 12 wk	12	All measurements after crossover	No
Witt et al.[43]	Low back pain	At 12 wk	12	All measurements after crossover	No
Brinkhaus et al.[4]	Low back pain	At 8 wk	8	End of treatment	No

Table 2

Sham-controlled acupuncture trials.

Trial name	Pain condition	Average length of treatment, wk	Time points after end of treatment	Included in meta-analysis
Carlsson and Sjölund[5]	Low back pain	8	Weeks 4, 12, and 26	Yes
Foster et al.[10]	Osteoarthritis	3	Weeks 3, 23, and 49	Yes
Guerra de Hoyos et al.[14]	Shoulder	8	Weeks 5 and 18	Yes
Irnich et al.[16]	Neck	3	Weeks 1 and 10	Yes
Kennedy et al.[18]	Low back pain	5	End of treatment and week 7	Yes
Kerr et al.[19]	Low back pain	6	None	No
White et al.[38]	Neck	4	End of treatment and weeks 1 through 8	Yes
Linde et al.[22]	Migraine	8	End of treatment and weeks 4 and 16	Yes
Melchart et al.[25]	Headache	8	End of treatment and weeks 4 and 16	Yes
Berman et al.[3]	Osteoarthritis	26	End of treatment	No
Kleinhenz et al.[20]	Shoulder	4	End of treatment	No
Diener et al.[8]	Migraine	6	End of treatment and weeks 7 and 20	Yes
Scharf et al.[27]	Osteoarthritis	6	Weeks 7 and 20	Yes
Haake et al.[15]	Low back pain	6	End of treatment and weeks 7 and 20	Yes
Endres et al.[9]	Headache	6	End of treatment and weeks 7 and 20	Yes
Vas et al.[32]	Osteoarthritis	12	Week 1	No
Vas et al.[34]	Neck	3	Weeks 1 and 25	Yes
Vas et al.[33]	Shoulder	3	Weeks 1, 10, 23, and 49	Yes
Witt et al.[40]	Osteoarthritis	8	End of treatment and weeks 18 and 44	Yes
Brinkhaus et al.[4]	Low back pain	8	End of treatment and weeks 18 and 44	Yes

To test whether the effects of treatment changed differently over time between the acupuncture and control groups, the analysis was repeated separately for each trial. The coefficients for the interaction term between treatment group and time since end of treatment were saved out along with the SE of the estimate and entered into a meta-analysis.

As a sensitivity analysis, this model was also used to perform a 1-stage meta-analysis for no acupuncture–controlled and sham-controlled trials separately. Data from all trials were included, and the model was also adjusted for trial.

To give a visual representation of how the effects of acupuncture change over time, the results are presented graphically in 2 ways: as standardized pain scores over time since randomization, and as standardized pain scores over time since the end of treatment. A longitudinal model for the effect of time on pain change score (including cubic splines with knots at the tertiles) was used to predict and graph pain change over time for the acupuncture and control groups separately.

3. Results

In most trials, patients received 8 to 15 treatments over 10 to 12 weeks. Only one trial had a longer treatment duration, 26 weeks.[3] A subset of studies recorded the number and frequency of sessions actually received by patients on the trial. In the acupuncture arm of trials with a no acupuncture control group, the mean number of treatments was 8 over 8 weeks (N = 444). For sham trials, the number and duration of treatment were similar for both the acupuncture and sham arms: a mean of 10 treatments over 6 weeks (N = 662).

3.1. Acupuncture compared with no acupuncture controls

In our analysis of acupuncture vs no acupuncture controls, a total of 8 trials and 2985 patients were included. The results of the meta-analysis for these 8 trials with no acupuncture controls are shown in **Figure 1**. Note that in this figure the weights are determined using inverse variance weighting, so for example if a trial had a small confidence interval (CI) (very low variance), it had a higher weight than other trials of the same or even larger sizes that had higher variances. Effect size is reported as a posttreatment change in SD per 3 months for the acupuncture trials compared with the no acupuncture–controlled trials. The fixed-effects estimate for the between-group comparison of acupuncture vs no acupuncture controls showed a nonsignificant decrease in the effect size of acupuncture of (0.011 SD per 3 months, 95% CI: −0.014 to 0.037, $P = 0.4$) after the end of treatment. As the difference between acupuncture and control has previously been found to be close to 0.5 SD,[35] the effect size of 0.011 SD per 3 months is equivalent to approximately a 9% diminution of treatment effects in the acupuncture vs no acupuncture group at 12 months. There was significant heterogeneity between trials ($P = 0.006$).

Figure 2 and Supplementary File Figure 1 (available online at http://links.lww.com/PAIN/A355) both show a trend of an increase in the effect of both acupuncture and no acupuncture groups over time, whereas the difference in the pain change scores between the 2 groups remains relatively consistent from randomization up to 1 year after the end of treatment. The effect sizes for the individual arms in these trials that report data beyond 6 months are presented in **Table 3**. The increase in overall effects in both arms might be attributable to the smaller effect sizes in the trial at 49 weeks[10] and the larger effect sizes of the trial with the longest follow-up at 92 weeks[30] (**Table 3**).

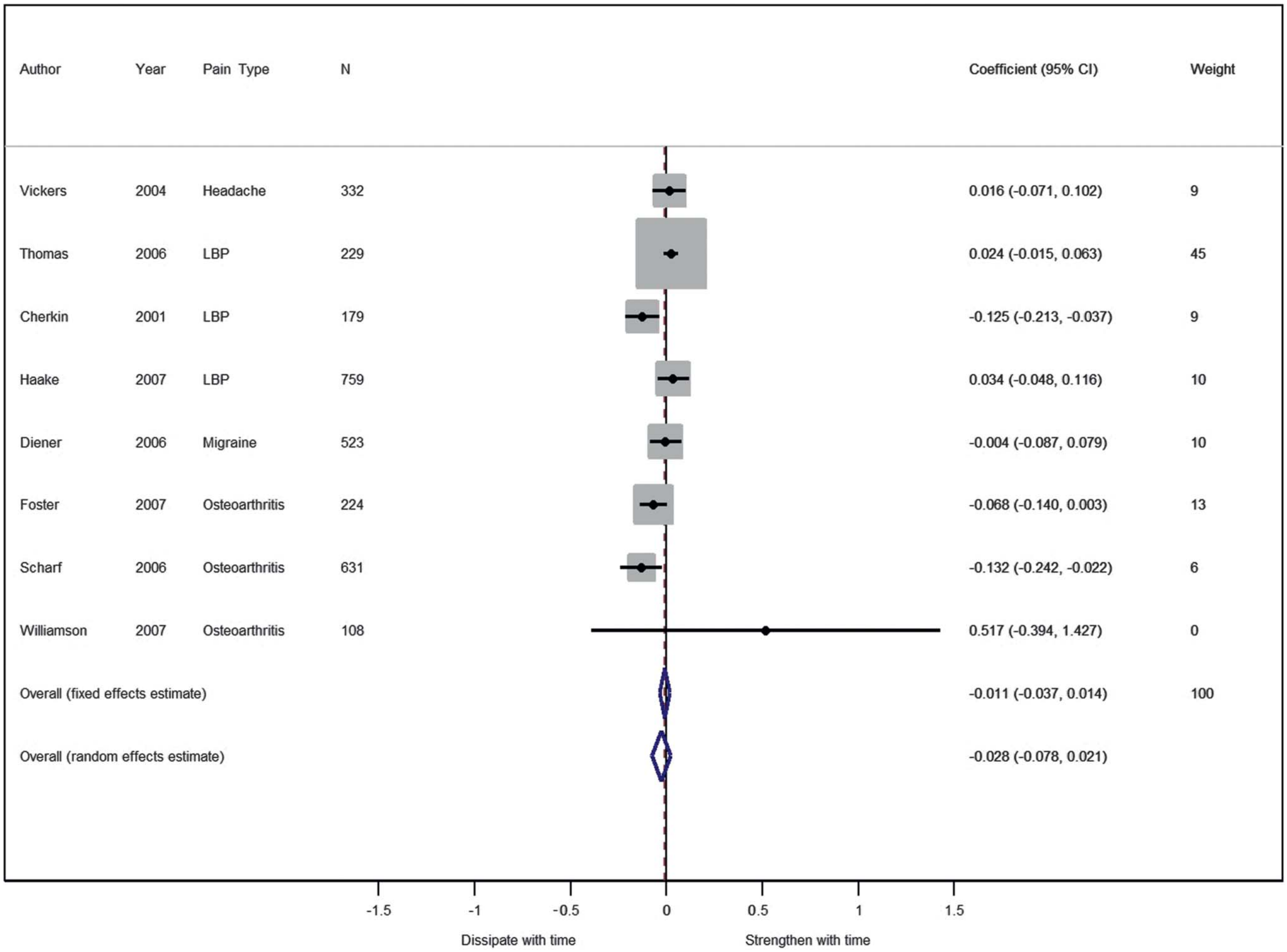

Figure 1. Forest plot showing the difference in pain change scores between acupuncture and no acupuncture control groups over time. A coefficient of 0.01 means that the difference between acupuncture and control increases by 0.01 SDs for each 3 months after the end of treatment. CI, confidence interval; LBP, low back pain.

We conducted a sensitivity analysis in which data were entered into a 1-stage meta-analysis. In the 1-stage approach, the longitudinal model described above was applied to a data set including all trials with a no acupuncture control group. The model incorporated the nonindependence between observations on a single patient and between observations on different patients in the same trial. Results for no acupuncture–controlled trials were almost identical to the 2-stage meta-analysis, with an overall reduction of 0.011 SD per 3 months, (95% CI: −0.034 to 0.013).

3.2. Acupuncture compared with sham acupuncture controls

We included a total of 16 trials and 4534 patients in our analysis for acupuncture-controlled vs sham-controlled trials. The results of the meta-analysis for these 16 sham acupuncture–controlled trials are shown in **Figure 3**. Among these trials, we found a significant reduction in pain change scores over time between the sham and acupuncture groups (effect size = −0.025 SD per 3 months, 95% CI: −0.050 to 0.000, P = 0.05) after the end of treatment. Because the difference between acupuncture and sham controls has previously been found to be close to 0.2 SD,[35] this reduction would mean about a 50% diminution of effect size for acupuncture compared with sham patients at 12 months. Significant heterogeneity was also seen in sham-controlled trials ($P < 0.0001$).

For all 3 neck pain trials[16,34,38] included in this analysis, the effects of acupuncture decreased over time compared with sham (**Fig. 3**), with 2 of these trials[34,38] showing a statistically significant decrease. In a sensitivity analysis that excluded neck pain trials, we found that there was a smaller nonsignificant reduction in how differences in pain between groups changed over time (effect size = −0.014, 95% CI: −0.039 to 0.011, P = 0.3) after treatment. Moreover, there was no longer significant heterogeneity between sham acupuncture–controlled trials (P = 0.2). When excluding these 3 neck pain trials from the analysis, the diminution of effect in acupuncture patients compared with sham is approximately 28% at 1 year, suggesting that most of the effects of acupuncture might persist over time for the nonneck–related chronic pain conditions. The Vas trial of acupuncture for shoulder pain[33] had a relatively large weight because outcome was measured 3 times after the end of treatment, allowing more precise estimates of the time course of treatment. However, excluding this trial had very little effect on the analyses (−0.024 SD per 3 months, 95% CI: −0.053 to 0.005).

For sham-controlled trials, the 1-stage meta-analytic approach found a slightly larger reduction in effect size compared with 2-stage meta-analysis (−0.036 SD per 3 months, 95% CI: −0.060 to −0.012). However, the principal findings were not importantly affected: there was a large reduction in effect for neck pain trials (−0.581 SD per 3 months, −0.736, −0.427) but reductions in

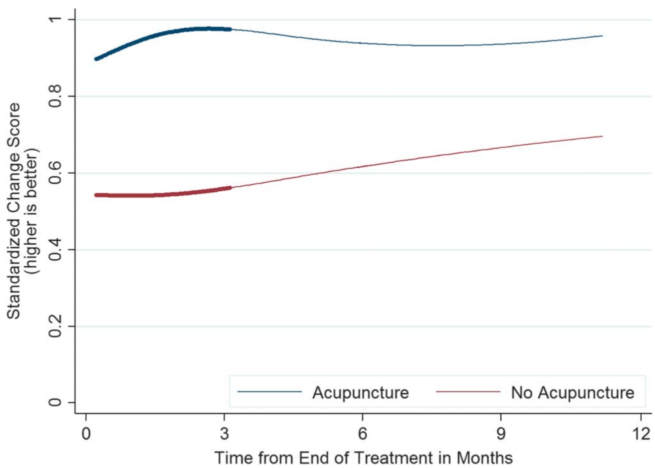

Figure 2. Effects of acupuncture and no acupuncture control over time since the end of treatment. Line thickness represents the number of trials contributing data at these time points: the thicker line represents 5 to 9 trials and the thinner line represents 2 to 4 trials.

effect size for trials on nonneck pain indications were nonsignificant (−0.021 SD per 3 months, 95% CI: −0.046 to 0.003).

The pain change scores in each group over time after the end of treatment are shown in **Figure 4**. Change scores after randomization are shown in Supplementary File Figure 2 (available online at http://links.lww.com/PAIN/A355). In the latter, the benefits of both acupuncture and sham acupuncture groups seem to be largely sustained over time, with the difference in the pain change scores between the 2 groups remaining relatively consistent up to 1 year after randomization. **Figure 4** shows a trend of a decrease in the effect of both the acupuncture delivered within a sham-controlled trial and the sham acupuncture over time. Among these sham-controlled trials, 1 trial reported larger effect sizes at 6 months after the end of treatment,[34] and 3 trials reported data nearer to 12 months after the end of treatment[4,10,40] (**Table 3**). The fact that the effect sizes in these 3 trials at 1 year after treatment are smaller overall than the trial with the large effect sizes reporting data at 6 months is likely to explain in part the observed decrease in treatment effect in sham-controlled trials over time.

3.3. Post hoc analyses

In light of our findings, we conducted a number of unplanned analyses. To determine whether the estimates of decrease in acupuncture effect relative to sham acupuncture or no acupuncture control are different, we compared the mean difference between acupuncture and each control group. We found no evidence of heterogeneity in how the effects of acupuncture dissipate between sham and no acupuncture–controlled trials when including all trials in the analysis ($P = 0.5$) or when excluding neck pain trials from the analysis ($P = 0.9$).

One reason why we may have failed to find significant reductions in acupuncture effects over time is that the analysis included trials irrespective of whether they reported differences between acupuncture and control. Obviously, a trial that showed no difference between groups cannot show a reduction in acupuncture effects over time. Hence, we repeated our analyses excluding trials that concluded no significant effect of acupuncture compared with sham or no acupuncture control. Five no acupuncture–controlled trials with 2059 patients found a significant effect of acupuncture compared with no acupuncture control. Among these trials, there was a nonsignificant increase in the effects of acupuncture relative to no acupuncture control

Table 3

Effect size in SD for trials with follow-up longer than 6 months.

Acupuncture and no acupuncture control arms					
Trial	**Arm**	**Week 40**	**Week 42**	**Week 49**	**Week 92**
Foster et al.[10]	No acupuncture	—	—	0.60	
	Acupuncture	—	—	0.55	
Thomas et al.[30]	No acupuncture	1.09	—	—	1.17
	Acupuncture	1.30	—	—	1.46
Cherkin et al.[6]	No acupuncture	—	0.91	—	
	Acupuncture	—	0.85	—	
Vickers et al.[37]	No acupuncture	0.42	—	—	
	Acupuncture	0.80	—	—	
Acupuncture and sham acupuncture arms					
Trial	**Arm**	**Week 23**	**Week 25/26**	**Week 44**	**Week 49**
Carlsson and Sjölund[5]	Sham		−0.30		
	Acupuncture		0.91		
Foster et al.[10]	Sham	0.61	—	—	0.68
	Acupuncture	0.56	—	—	0.57
Vas et al.[34]	Sham	—	1.03	—	—
	Acupuncture	—	1.59	—	—
Vas et al.[33]	Sham	0.33	—	—	0.52
	Acupuncture	1.02	—	—	1.22
Witt et al.[40]	Sham		—	0.72	—
	Acupuncture		—	0.78	—
Brinkhaus et al.[4]	Sham		—	0.69	—
	Acupuncture		—	0.76	—

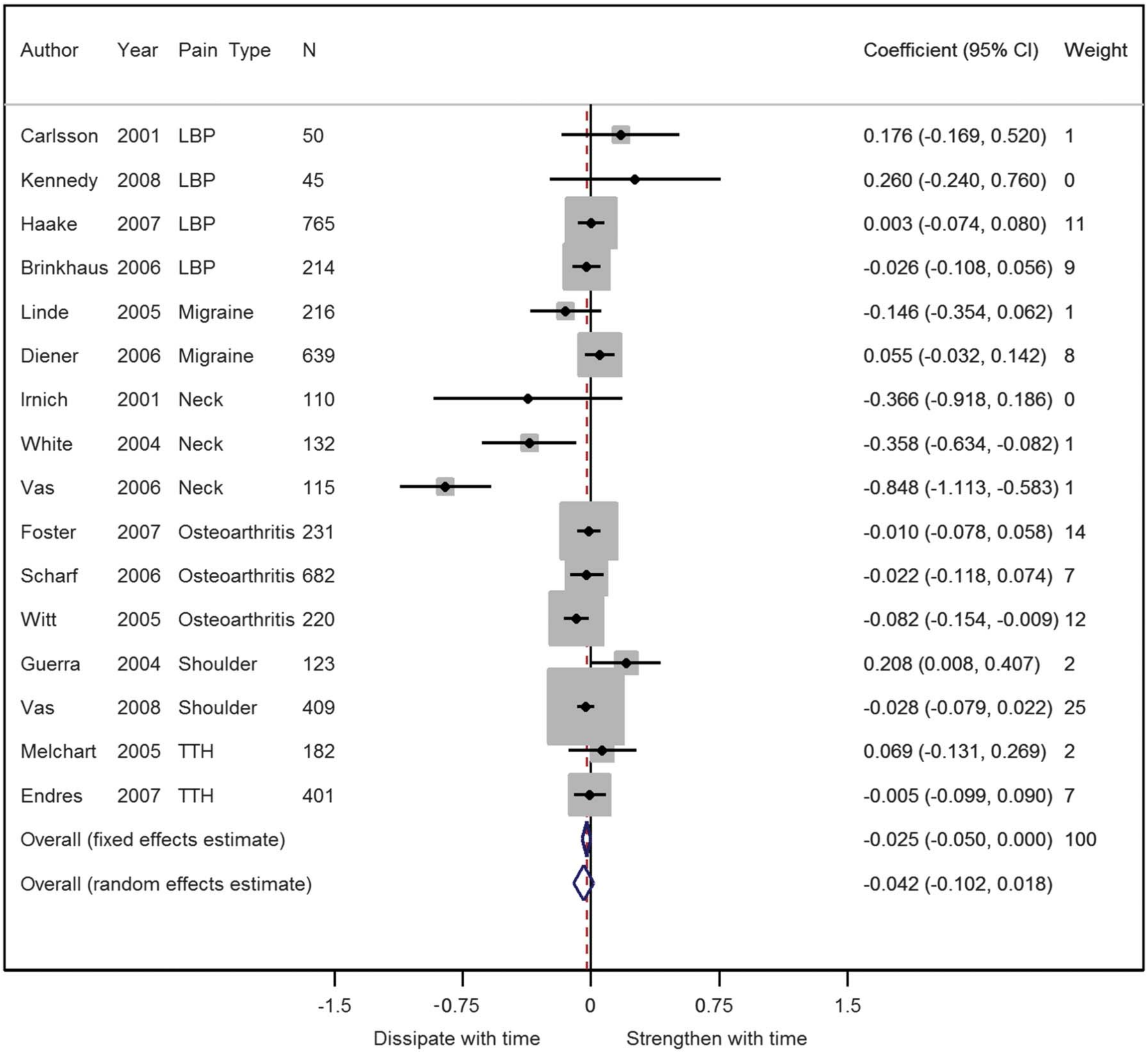

Figure 3. Forest plot showing the difference in pain change scores between acupuncture and sham control groups over time. A coefficient of 0.01 means that the difference between acupuncture and control increases by 0.01 SDs for each 3 months after the end of treatment. CI, confidence interval; LBP, low back pain; TTH, tension-type headache.

(0.013 SD per 3 months, 95% CI: −0.018 to 0.44, $P = 0.4$). There were 7 sham-controlled trials with 1450 patients that found a significant effect of acupuncture compared with sham acupuncture. There was a significant decrease in the effects of acupuncture relative to sham for every 3 months of follow-up of 0.049 SD (95% CI: −0.086 to −0.013, $P = 0.008$) and significant heterogeneity between trials ($P < 0.0001$). Excluding neck pain trials from this sensitivity analysis left 5 trials with 1203 patients. There was no longer significant heterogeneity ($P = 0.060$), and the decrease in the effect of acupuncture compared with sham was smaller and no longer significant when excluding both neck pain trials and trials that found no effect of acupuncture relative to sham: a decrease of 0.028 SD for every 3 months of follow-up (95% CI: −0.065 to 0.009, $P = 0.13$).

When including all trials that found an effect of acupuncture, there was significant heterogeneity, with the effects of acupuncture decreasing much more rapidly in the sham acupuncture trials than in the no acupuncture–controlled trials ($P = 0.011$). However, when excluding the neck pain trials from this analysis, we found a nonsignificant reduction in the effects of acupuncture over time between the sham-controlled and no acupuncture–controlled trials that found a significant effect of acupuncture ($P = 0.097$).

To explore these results further, we repeated our analyses separately for neck pain and compared our findings to other pain patient subgroups combined. The estimate of a reduction in neck pain treatment benefit of 0.587 (95% CI: 0.406-0.767) SDs per 3 months is very much higher than the estimate of 0.014 (95% CI: −0.039 to 0.011) for comparison conditions ($P < 0.0001$). On closer inspection of data from each trial, improvements from baseline in the acupuncture group were stable in 1 trial at 8 weeks postrandomization[38] but decreased by 40% to 50% in 2 trials with 10 to 25 weeks additional follow-up.[16,34]

4. Discussion

4.1. Principal findings

The effects of acupuncture compared with no acupuncture for chronic pain do not seem to decrease importantly over a projected 12-month period. We did not see a statistically significant association with time. The central estimate suggests that approximately 90% of the benefit of acupuncture relative to controls would be sustained at 12 months, or when using the upper bound of the CI, approximately 70% of the benefit

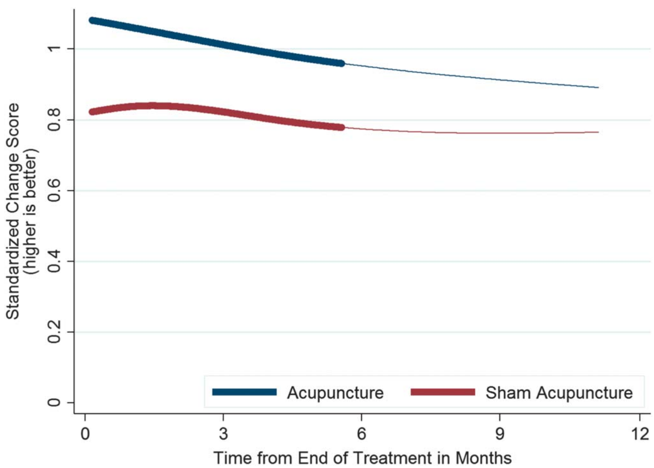

Figure 4. Effects of acupuncture and sham acupuncture control over time since the end of treatment. Line thickness represents the number of trials contributing data at these time points: the thicker line represents 10 or more trials and the thinner line represents 2 to 4 trials.

of acupuncture relative to controls would be sustained at 12 months.

The results for acupuncture vs sham were similar after exclusion of studies on neck pain. We did see clear evidence that the effects of acupuncture vs sham on neck pain do diminish over time. When excluding neck pain trials from the analysis to reduce heterogeneity, the diminution of effect in acupuncture patients compared with sham was approximately 30% at 1 year, suggesting that much of the effects of acupuncture persist over time for the nonneck–related chronic pain conditions. This might be explained in part by the shorter courses of treatment provided in the neck pain trials,[16,34,38] which were in the range of 3 to 4 weeks, in contrast to the more commonly provided courses lasting 6 to 8 weeks or longer for the other conditions (**Table 2**).

4.2. Strengths and limitations

The key strength of this study is that we have used a meta-analysis drawing on an individual patient's data from high-quality randomized controlled trials of acupuncture for chronic pain, which found that acupuncture was superior to both sham and no acupuncture controls for each pain condition.[35] Using this large data set of nearly 18,000 patients, we have been able to explore subgroups with a precision not possible when using only summary trial data, as would be the case when using conventional meta-analytic methods. A key limitation was that not all trials in the data set provided data at more than one post-treatment follow-up. We only have data from 8 of the 20 trials that followed patients for 40 weeks or more. One trial provided follow-up at 2 years after randomization.[22] We do believe it is reasonable to draw conclusions about the time course of acupuncture effects over a 1-year period. First, the data that we do have from trials with longer term follow-up do indeed suggest persistence of effects, incidentally a characteristic that may not be unique to acupuncture. Second, we did not see any difference on how treatment benefit changed over time comparing trials with longer vs shorter follow-up, which is why we used data from all trials to estimate the effects of time on treatment. It would be incorrect to conclude that "no important diminution of effect at 12 months" means "effects persist well beyond 12 months."

4.3. Relationship to the wider literature

Our conclusions as to the time course over which acupuncture seems to provide benefits differ to some extent from data reported in a number of previous systematic reviews of acupuncture for chronic pain based on summary.[1,2,7,11,12,13,21,23,28,29,31] The critical difference between the current article and previous reviews is that the latter reviews did not directly evaluate the time course of acupuncture effects. When a previous review reports that results were significant at an early time point, but not at a later time point, this cannot be taken as evidence that results changed over time. There are several reasons why significance may change even if underlying effects do not. The most obvious is if the number of patients changes over time due to drop out. For instance, a trial with 150 patients per group and a 0.25 SD difference between groups at posttreatment would be statistically significant ($P = 0.031$). If results were identical at a 6-month follow-up, but 25% of patients dropped out, the P value would be 0.063. Alternatively, if there was no drop out and no changes in mean pain scores, but longer follow-up was associated with a 25% increase in SD, perhaps associated with greater variability of pain over time, the P value would again be nonsignificant ($P = 0.084$). In both cases, the effects of treatment persist, and an analysis directly testing trends over time would confirm this finding; taking the approach of the conventional reviews and indirectly assessing change over time by separate inference at different time points would lead to incorrect conclusions regarding the time course of underlying effects. We are the first systematic review to directly analyze change over time using appropriate methods for longitudinal data.

Differences between our results and the previously published systematic reviews can be illustrated by taking as an example the review by Furlan et al.[12] who found that "acupuncture did not significantly differ from placebo in improving pain intensity scores" for low back and neck pain. In our meta-analysis, we used different inclusion criteria to select trials for review, which included the multiple pain conditions of headache/migraine, osteoarthritis, and low back and neck pain, whereas Furlan only included low back and neck pain. Our more strict inclusion criteria required evidence of unambiguous allocation concealment, leading to our inclusion of only higher quality trials, which are less likely to be susceptible to bias. The critical difference, however, between the analysis we present here and the analyses of Furlan et al. is that they did not directly address the time course of acupuncture effects. Their analyses were limited to those trials that measured similar outcomes during approximately the same periods. We obtained patient data from all eligible trials and performed an individual patient data meta-analysis within which we were able to standardize and compare multiple types of outcome. Because we had individual patient data, we were able to incorporate outcomes measured at all time points from all trials into one analysis, rather than drawing conclusions from multiple separate analyses and we therefore conducted an analysis that directly addressed the question at hand.

4.4. Implications for research and practice

The major clinical implication of our findings is that we can reassure chronic pain patients considering acupuncture that any treatment benefit does persist after the end of treatment. This is naturally also a consideration for other clinicians who may refer patients for acupuncture. A concern for such clinicians and their patients is that they may go through the time, trouble, and expense of a course of acupuncture treatment, but then regress to having the same amount of pain shortly after treatment ends.

This cannot be assumed, given the evidence that the effects of acupuncture for chronic pain persist for at least a year. A possible exception is neck pain, as we saw some evidence that differences between acupuncture and sham decrease over time for this condition.

Our findings also have implications on cost-effectiveness studies that use utility measures. Such studies calculate benefit, in terms of increase in quality-adjusted life years (QALYs) associated with an intervention, and divide by the increase in cost associated with that intervention. Increase in QALYs depends on a "time horizon" for treatment effectiveness. In many cost-effectiveness studies on acupuncture, this time horizon is given as the length of follow-up, effectively assuming that the benefits of acupuncture disappear completely the moment that a patient completes their final questionnaire or follow-up assessment. Changing the time horizon dramatically impacts cost-effectiveness. In the case of a trial with the final follow-up at 3 months, but using a time horizon of 12 months (a minimum based on our data) rather than a time horizon of 3 months, would reduce the cost per QALY by 75%.

In terms of future prospective research, it is clear that further studies should continue to measure outcomes beyond the end of acupuncture treatment, at least at 12 months follow-up and, ideally, beyond. In one Acupuncture Trialists' Collaboration study,[37] the average duration of chronic pain in the study cohort was over 20 years. It surely behoves the research community to adequately fund studies to assess long-term outcomes in patients with chronic pain. Given the discrepant results for chronic neck pain, future studies could focus specifically on the time course of acupuncture for this type of pain. Moreover, there is a case for exploring the biological plausibility of physiological changes in substudies embedded within clinical trials to provide a mechanistic explanation of the longer terms benefits associated with acupuncture. It is also plausible that the sustained effects of acupuncture may be explained by, as yet unspecified and unmeasured, treatment-mediating factors.

5. Conclusions

With the possible exception of neck pain, the effects of acupuncture compared with no acupuncture for chronic pain do not seem to decrease importantly over 12 months. Patients can generally be reassured that treatment effects are likely to persist. Cost-effectiveness studies should take our findings into account when considering the time horizon of acupuncture treatment. Further research should measure long-term outcome of acupuncture for patients with chronic pain.

Conflict of interest statement

The authors have no conflicts of interest to declare.

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Appendix A. Supplemental Digital Content

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