

Acupuncture in Chronic Pain



The problem with Sham Acupuncture

Dr Mike Cummings

XV Congreso

SOCIEDAD ESPAÑOLA DEL DOLOR

24-26 mayo 2018
Palma de Mallorca

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Medical Director BMAS
Director of Education BMAS
Associate Editor *Acupuncture in Medicine*
Honorary Clinical Specialist UCLH

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Mike is Medical Director of the British Medical Acupuncture Society (BMAS). This is a full time post that involves running the BMAS London Teaching Clinic (LTC), co-ordinating and lecturing on BMAS courses in Western medical acupuncture, acting as an associate editor for the Medline-listed journal *Acupuncture in Medicine*, and representing the BMAS at various academic and political meetings. Mike is an Honorary Clinical Specialist at the Royal London Hospital for Integrated Medicine, which is part of the University College London Hospitals NHS Foundation Trust, where he supports acupuncture services.

His principal academic and clinical interest is musculoskeletal pain, and in particular, needling therapies in the treatment of myofascial pain syndromes.

After completing his medical degree at Leeds, and several hospital jobs in the north of England, Mike joined the Royal Air Force for a six and a half year short service commission. A substantial portion of the workload for a general duties medical officer (GDMO) in the RAF is musculoskeletal medicine. Mike came across acupuncture by accident whilst working as a GDMO. He followed his interest in musculoskeletal medicine and acupuncture on retiring from military service, and finally found himself occupied full time in the field of acupuncture (see start of the piece).

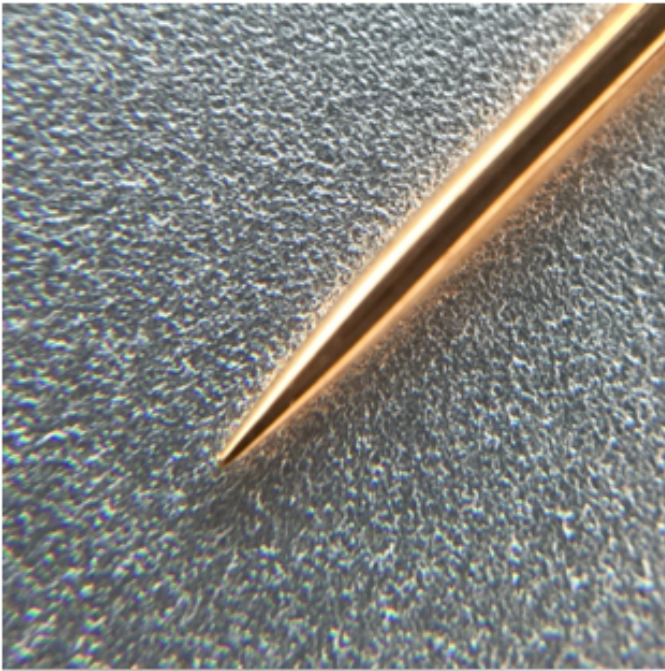
Read Mike's profile in the Leeds University Medical School Alumni magazine from 2003.

Read a description of how Mike unexpectedly got into acupuncture in Toby Murcott's book - *The Whole Story* from 2005.

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Dr Mike Cummings MB ChB DipMedAc

Musculoskeletal Physician
Medical Acupuncturist

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Declaration of interests

I am the salaried [medical director](#) of the [British Medical Acupuncture Society \(BMAS\)](#), a membership organisation and charity established to stimulate and promote the use and scientific understanding of acupuncture as part of the practice of medicine for the public benefit.

I am an [associate editor](#) for [Acupuncture in Medicine](#).

I have a very modest private income from lecturing outside the UK, royalties from textbooks and a partnership teaching veterinary surgeons in Western veterinary acupuncture. I have no private income from clinical practice in acupuncture. My income is not directly affected by whether or not I recommend the intervention to patients or colleagues, or by whether or not it is recommended in national guidelines.

I have not chaired any NICE guideline development group with undeclared private income directly associated with the interventions under discussion. I have participated in a NICE GDG as an expert advisor discussing acupuncture.

I have used Western medical acupuncture in clinical practice following a chance observation as a medical officer in the Royal Air Force in 1989. My opinions are formed by data that spans the range of quality and reliability, much of which is in the public domain.

I have a logical mistrust of the motives of anyone who advertises an interest or hobby in being a 'Skeptic', as opposed to using appropriate scepticism within their primary profession, or indeed organisations that claim to promote generic 'science' as opposed to actually engaging in it.

Disclosure – no conflict of interest
mike.cummings@btinternet.com
goo.gl/6XQeXv

Medicine (Leeds) 1987
Musculoskeletal Medicine
RAF Medical Officer 1989–96
Acupuncture 1993–
Director of Education BMAS 1997–
Editor *Acupuncture in Medicine* 1999–
Medical Director BMAS 2001–
Expert Adviser NICE CG88 2007–09



From an early age I was interested in somatic anatomy and of musculoskeletal physiology. I continued that interest through medical school and beyond. Acupuncture was a chance discovery whilst serving as a medical officer in the British military. After retiring from the Royal Air Force, my career took a path that was guided by my interest in musculoskeletal pain and strongly influenced by taking over an acupuncture practice that was formerly run by Dr Adrian White. At the time Adrian was the president of the British Medical Acupuncture Society (BMAS), and when I took over his practice, he went into research at Exeter University. I continued my interest in clinical medicine, but at the same time was inducted into the world of systematic reviews and publishing. I kept a foot in both camps, and this has served me well in my position as medical director of the BMAS.

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Publications

- 81 total publications
- 67 in peer reviewed journals
- 4 systematic reviews
- 1 Cochrane review
- 10 textbook chapters
- 4 textbooks



The full list of references can be found here: goo.gl/6XQeXv

Acupuncture in Chronic Pain

Topics

- ❖ What is sham acupuncture and why use it? ←
- ❖ the Modellvorhaben Akupunktur
- ❖ Vickers IPDM 2012
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- ❖ Conclusions

Fritillaria imperialis
Royal Botanical Gardens
Kew

Fritillaria imperialis is a species of flowering plant in the lily family, native to a wide stretch from Kurdistan across the plateau of Turkey, Iraq and Iran to Afghanistan, Pakistan and the Himalayan foothills.

It grows to about 1m in height, and bears lance-shaped, glossy leaves at intervals along the stem. It bears a prominent whorl of downward facing flowers at the top of the stem, topped by a 'crown' of small leaves, hence the name. While the wild form is usually orange-red, various colours are found in cultivation, ranging from nearly a true scarlet through oranges to yellow. The pendulous flowers make a bold statement in the late spring garden; in the northern hemisphere, flowering takes place in late spring, accompanied by a distinctly foxy odour that repels mice, moles and other small animals.

Due to the way that the bulb is formed, with the stem emerging from a depression, it is best to plant it on its side, to prevent water causing rot at the top of the bulb.

This photo was taken at the Royal Botanical Gardens in Kew on 14 April 2018.

I placed the camera on the grass as an experiment to avoid including the crowds of admiring visitors.

Two black dots in the sky were captured by accident, as the shutter was on a 10 second delay. The fatter blob on the left is a bee flying over the flowers, and the thinner black object on the right is a commercial aircraft on a westerly approach to land at Heathrow airport.

Canon EOS 5D Mark III

Canon EF24-70mm f/2.8L II USM

Taken at f/8.0 24mm 1/250 iso100

What is Sham acupuncture?

- Sham acupuncture is used in randomized double-blind controlled trials so that participants do not know whether or not they have received the real treatment...
- sham means fake, or not the real thing
- sham acupuncture is intended to look like acupuncture but without any of the real effect of acupuncture
- BUT, is this possible to achieve?

What is Sham acupuncture?

- Sham acupuncture is used in randomized double-blind controlled trials so that participants do not know whether or not they have received the real treatment...

○ Sham acupuncture techniques:	Active?	Adequacy?
◇ Off-point acupuncture	yes	good
◇ Wrong point	yes	good
◇ Minimal needling	partially	good
◇ Non-penetrating device	minimally	limited areas
◇ Non-penetrating needle		
• Standard needle	no	limited areas
• Retractable needle	partially	impedes real
• Double blind device	no	impedes real
◇ Mock TENS	no	unlikely
◇ Sham laser	no	unlikely



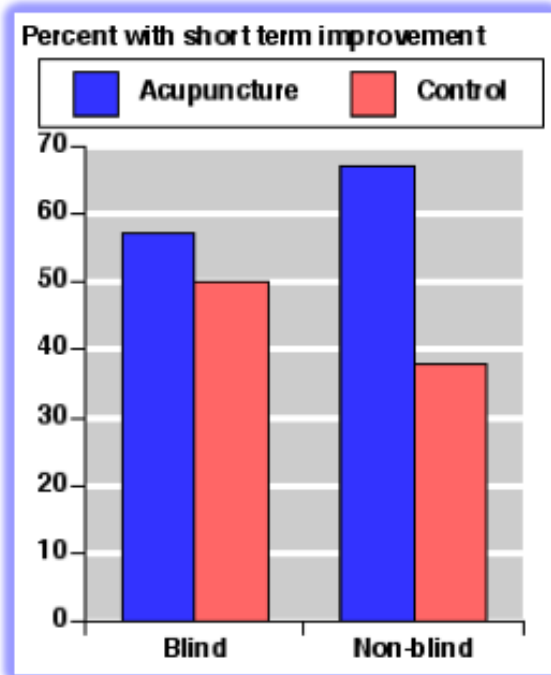
This list is taken from Cummings, M., & White, A. (2016). A Critical Approach to Randomised Controlled Trials of Acupuncture. In J. Filshie, A. White, & M. Cummings (Eds.), *Medical Acupuncture – A Western Scientific Approach* (2nd ed., pp. 279–297). London: Elsevier.

Why use Sham acupuncture?

- Sham acupuncture is principally used to avoid detection bias
 - ✧ Detection bias is systematic differences between groups in how outcomes are determined
 - ✧ Blinding (or masking) of outcome assessors may reduce the risk that knowledge of which intervention was received, rather than the intervention itself, affects outcome measurement.
 - ✧ Blinding of outcome assessors can be especially important for assessment of subjective outcomes, such as degree of postoperative pain.
 - Cochrane Handbook for Systematic Reviews of Interventions

Why use Sham acupuncture?

Effect of blinding on outcome of trials of acupuncture for chronic back pain.
Bandolier 80 2000;7(10):2.



There is a little story that accompanies this slide.

Bandolier was a publication on evidence-based medicine produced by Andrew Moore who worked out of the Pain Research Unit in Oxford.

He was notorious for his dislike of all CAM interventions including acupuncture. He published a piece about bias and used data from a systematic review of acupuncture studies in back and neck pain to illustrate the effect of bias in unblinded trials, but without any discussion of how you achieve blinding. I emailed him and suggested we should use the placebo for acupuncture in the blinded studies in our clinical practice as it seemed to work in 50% of patients (cLBP) and as a placebo must surely be entirely safe. The same author had previously written in a small textbook of pain that effective treatments in chronic pain worked about 50% of the time.

He replied to be: "You are missing the point, they would have got better on their own."

Evidence based medicine

- Evidence based medicine (EBM) is the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients.

Sackett DL, Rosenberg WM, Gray JA, *et al.* Evidence based medicine: what it is and what it isn't. *BMJ* 1996; 312(7023):71-72.

BMJ 1996;312:71-72 (13 January)

Editorials

Evidence based medicine: what it is and what it isn't

Evidence based medicine is the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients.

The practice of evidence based medicine means integrating individual clinical expertise with the best available external clinical evidence from systematic research.

By best available external clinical evidence we mean clinically relevant research, often from the basic sciences of medicine...

Good doctors use both individual clinical expertise and the best available external evidence, and neither alone is enough.

Without clinical expertise, practice risks becoming tyrannised by evidence...

Evidence based medicine is not restricted to randomised trials and meta-analyses.

The term 'evidence based medicine' was first used in the title of a paper (listed on PubMed) in 1992 (Guyatt et al JAMA 1992)

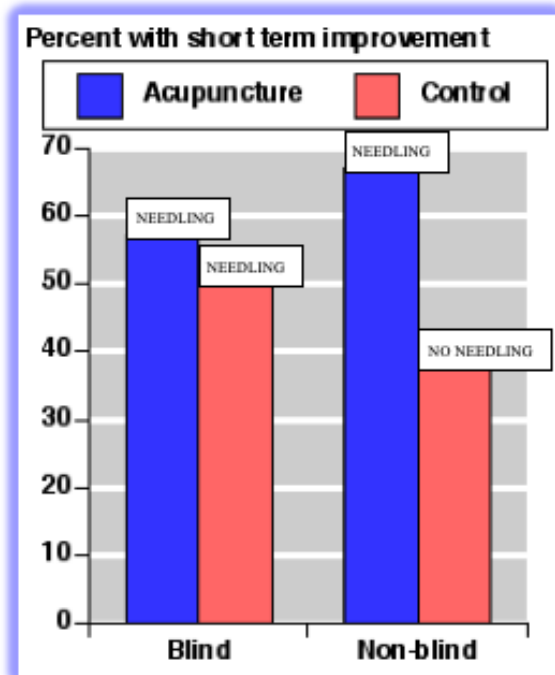
Evidence-based medicine: A new approach to teaching the practice of medicine.

The first systematic reviews in acupuncture were published in 1989, and the early years of reviewing were marked by changes in methodology. Reviewing became more and more a job for professional researchers who often were non-clinical. Clinical expertise was often marginalized, and this was particularly true in the field of acupuncture.

By chance, my career path had put me in an ideal position to try to bridge the gap between clinical practice and the new field of EBM.

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He replied to be: "You are missing the point, they would have got better on their own."

I was invited to speak at an event in the Royal Institution some years later, and Andrew Moore was there with this same slide.

I was able to recall his slide and describe our prior conversation, and then give an alternative explanation for the difference ie that all patients in the blinded studies received some form of needling.

The labels on top of each column have been added by me to the original diagram.

After the audience had finished laughing (at the way I described the story), Andrew leaded over to me and said: "Are you sure they were all needled in the control groups [of the blinded trials]."

I replied: "Yes, but you did the systematic review! You should have read the methods section."

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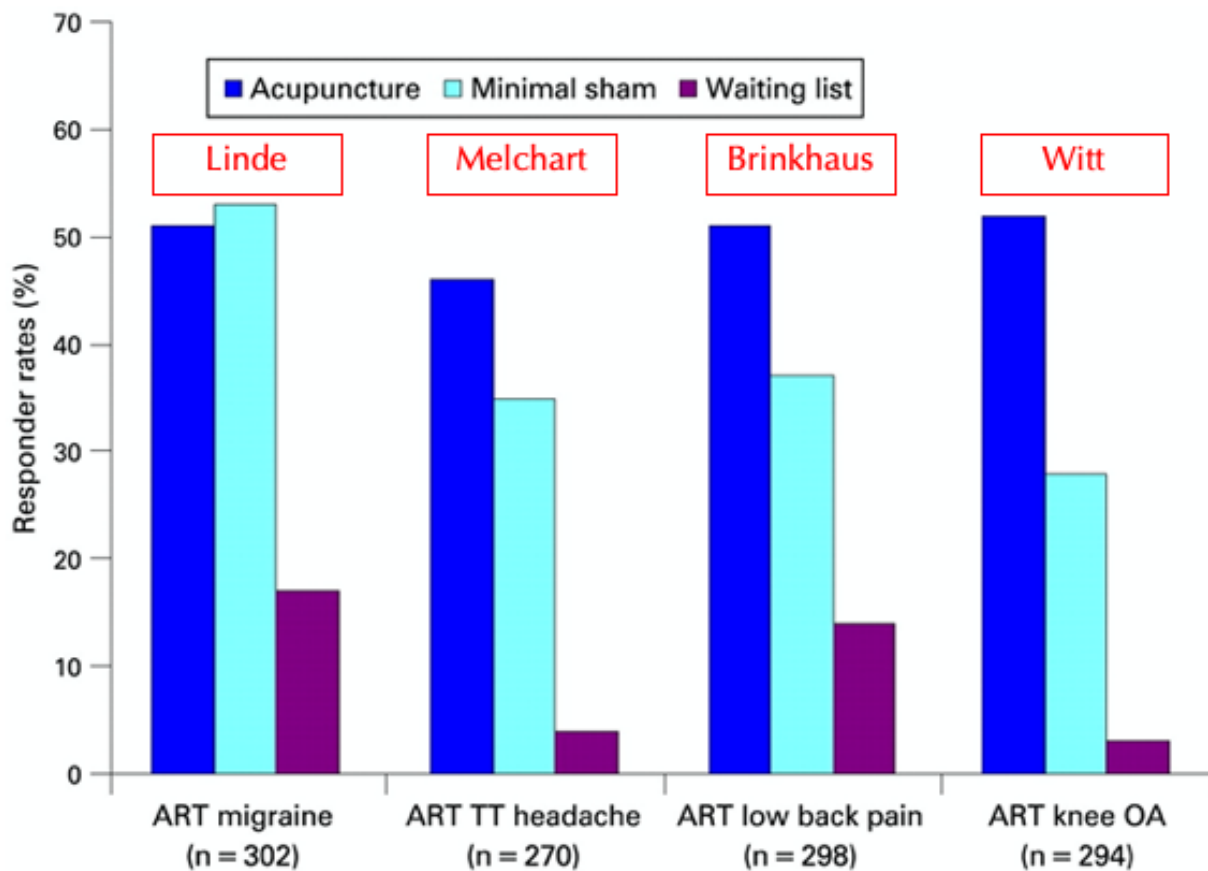
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Three large research programmes investigating the efficacy, effectiveness, cost effectiveness and safety of acupuncture treatment for certain chronic conditions ('Modellvorhaben Akupunktur') have been conducted in Germany since October 2000. These programmes were initiated after the German Federal Committee of Physicians and Health Insurers determined, in October 2000, that the scientific evidence supporting the use of acupuncture was not sufficient to justify routine reimbursement within the German healthcare system. Formerly, some of the cost of acupuncture treatment was covered by the German statutory health insurance funds, provided that the acupuncture was performed by physicians with at least 140 hours of acupuncture training.

Following the decision of the German Federal Committee of Physicians and Health Insurers in October 2000, reimbursement for acupuncture treatment was only possible for patients suffering from certain chronic conditions (knee osteoarthritis, low back pain, migraine, tension-type headache), and only if the physician performing the acupuncture participated in one of the three research programmes. The results discussed in this paper are from the controlled trials that made up the core of these research programmes: the Acupuncture Randomised Trials (ART), the Acupuncture in Routine Care studies (ARC), one comparative trial (COMP), and the German Acupuncture trials (GERAC).

These *Modellvorhaben* (trial phases) were funded by a number of the German statutory health insurance funds, and they were organised by groups of researchers and physicians based at three large German universities: the Charité University, Berlin (ART and ARC); the Technical University, Munich (ART and COMP); and the University of Bochum (GERAC).

Figure 1 Responder rates in the Acupuncture Randomised Trials (ART) trials after 8 weeks from baseline (9-12 weeks in ART migraine and tension-type (TT) headache); responder rates were defined (post hoc) as a 50% or greater reduction in the primary outcome measure. Acupuncture and minimal acupuncture were significantly superior to waiting list in all trials. Acupuncture was superior to minimal acupuncture only in ART knee osteoarthritis (OA).



Cummings, M. *Acupunct Med* 2009;27:26-30

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ART

These were four RCTs with roughly 300 subjects in each. They were performed principally as efficacy trials in four conditions: migraine; tension-type headache; chronic low back pain; and osteoarthritis of the knee. Each of the trials followed the same design: three parallel arms with a 2:1:1 distribution of subjects, so that there were approximately 150 subjects in the real (verum) acupuncture arm, and 75 in the others – the minimal acupuncture and waiting list arms. The acupuncture involved deep needling to classical acupuncture points with manipulation of the needles to produce de qi – a characteristic needling sensation. Twelve treatments were given over eight weeks. Minimal acupuncture involved superficial needling to standardised sites that were not near to any recognised acupuncture points. The waiting list group received acupuncture 2 or 3 months after randomisation ie after the data were collected for the primary outcome.

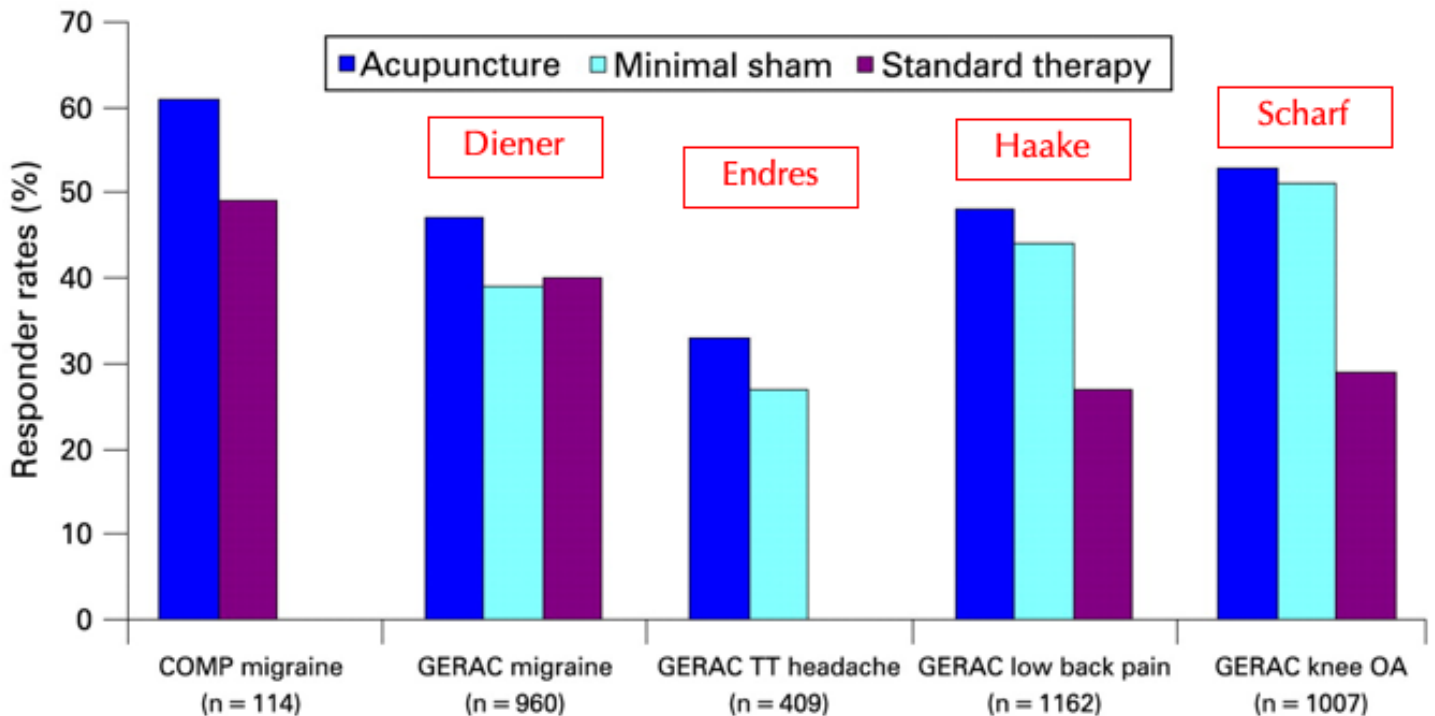
The primary outcomes were short term, just after the interventions at around 8 weeks, although outcomes were also assessed at 26 and 52 weeks from baseline.

The primary outcome for ART migraine was the difference in number of days with headache of moderate or severe intensity between the four weeks before randomisation (baseline phase) and weeks 9 to 12 after randomisation. Responders were defined (post hoc) as those with a 50% reduction or greater in days with moderate or severe pain (headache). The primary outcome and responder rates for ART tension-type headache were the same, with an additional comment that patients with missing data were automatically counted as non-responders.

The primary outcome in ART low back pain was the change in low back pain intensity from baseline to the end of week eight after randomisation, as measured by a visual analogue scale (range, 0-100 mm), and responders were defined (post hoc) by at least 50% reduction in pain intensity. Finally, the primary outcome measure in ART knee osteoarthritis was the change in the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) between baseline and week eight after randomisation, and responders were defined (post hoc) by a decrease of at least 50% in their WOMAC index score.

The ART programme trials were performed across between 18 and 30 outpatient centres across Germany: ART migraine 18; ART tension-type headache 28; ART low back pain 30; ART knee osteoarthritis 28.

Figure 2 Responder rates in the comparative trial (COMP) at 9-12 weeks from baseline, and the German Acupuncture trials (GERAC) at 6 months from baseline; responder rates were defined as: $\geq 50\%$ reduction in migraine days (COMP and GERAC migraine); $> 50\%$ reduction in headache days (GERAC tension-type (TT) headache); $\geq 33\%$ improvement on Chronic Pain Grade Scale questionnaire (CPGS) or $\geq 12\%$ improvement on the Hanover Functional Ability Questionnaire (GERAC low back pain); and $\geq 36\%$ improvement in Western Ontario and McMasters Universities Osteoarthritis Index (GERAC knee osteoarthritis (OA)). Acupuncture and sham acupuncture were both significantly superior to standard therapy in GERAC low back pain and GERAC knee OA. There were no other statistically significant differences between groups.



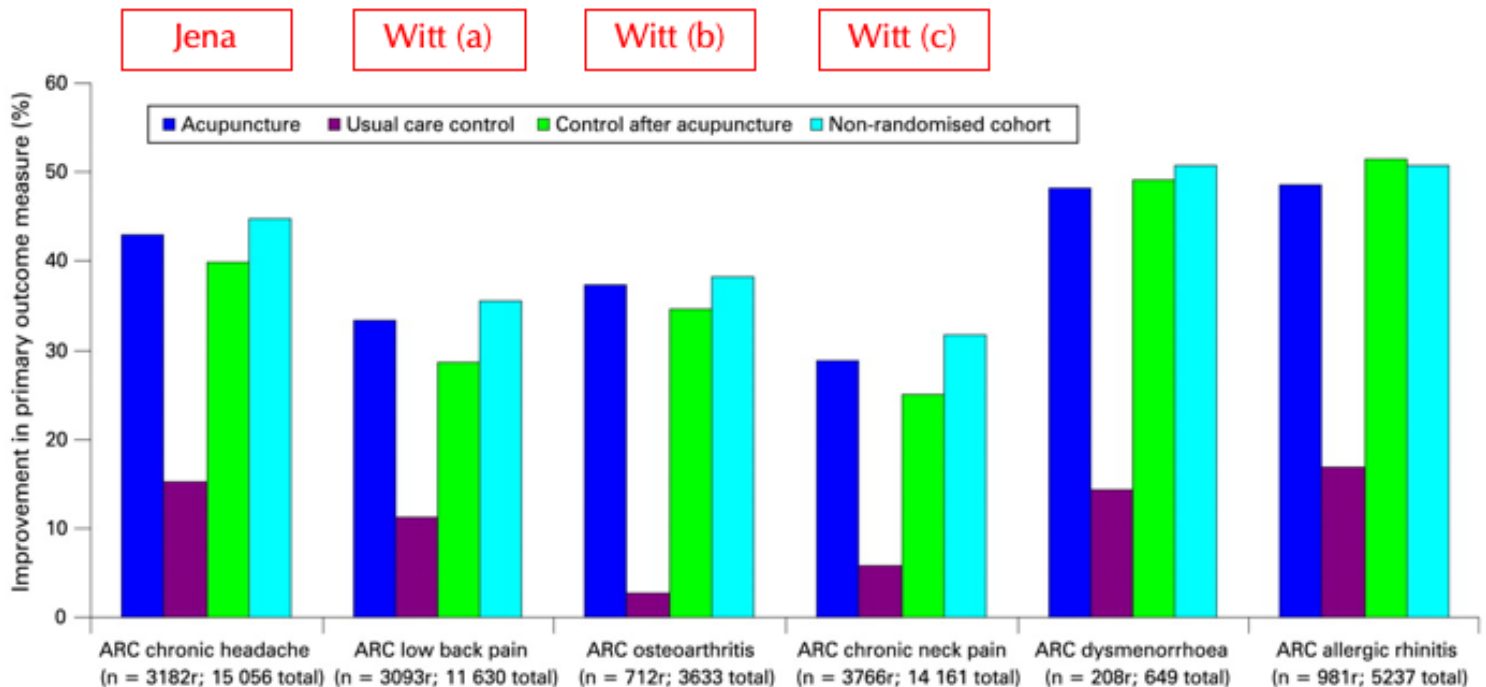
GERAC

There were four GERAC trials with up to 1000 subjects in each. They were designed as comparative trials with three equal parallel arms: acupuncture vs sham acupuncture vs standard care (note that the terminology: 'sham' is used rather than 'minimal'). They were performed in migraine, tension-type headache, chronic low back pain, and knee osteoarthritis. Rather like the ART trials, the real acupuncture involved deep needling to classical acupuncture points with manipulation of the needles to produce de qi. Ten treatments were given over six weeks, with the option to extend treatment by a further five sessions for partial response. Sham acupuncture involved superficial needling to standardised sites that were not near to any recognised acupuncture points. The standard care arms used best conventional care based on guidelines where available: GERAC migraine – beta blockers first choice, flunarizine second, valproic acid third; GERAC tension-type headache – the intention was to use amitriptyline; GERAC chronic low back pain – multimodal treatment programme including physiotherapy, exercise and NSAIDs; GERAC knee osteoarthritis – physiotherapy, physician visits, NSAIDs (in this trial all groups had six sessions of physiotherapy, and acupuncture groups were allowed limited NSAIDs as rescue medication).

The primary outcomes were measured around six months from baseline, although secondary outcomes were measured at six weeks and three months as well. The primary outcome in GERAC migraine was the difference in migraine days between four weeks before randomisation and weeks 23–26 after randomisation, and response was defined as a reduction in the number of migraine days by 50% or more. GERAC tension-type headache was somewhat different in that the response (defined as $> 50\%$ reduction in number of headache days per four weeks from baseline to six months) was the primary outcome, and all minor variations from protocol resulted in patients being classified as non-responders. In GERAC low back pain the primary outcome was response after six months, defined as 33% improvement or better on three pain related items on the Von Korff Chronic Pain Grade Scale questionnaire (CPGS) or 12% improvement or better on the back specific Hanover Functional Ability Questionnaire (HFAQ). Patients who were unblinded or who used (disallowed) co-interventions during follow up were classified as non-responders regardless of symptom improvement. In GERAC knee osteoarthritis the effect on pain and function was measured with the WOMAC score (total score and the subscales were standardised to 0 to 10). 'Success' rates were calculated according to a change of at least 36% from baseline WOMAC scores at 13 and 26 weeks after the start of treatment. Patients with missing data were considered to have had treatment failure.

The GERAC trials were performed across between 122 and 340 practices across Germany: GERAC migraine 149; GERAC tension-type headache 122; GERAC chronic low back pain 340; GERAC knee osteoarthritis 315.

Figure 3 Percentage improvement in the primary outcome measure at 3 months from baseline in the Acupuncture in Routine Care (ARC) trials ("control after acupuncture" is 6 months from baseline -- 3 months usual care followed by 3 months acupuncture treatment). Numbers in brackets are those randomised (r) followed by the total sample including the non-randomised cohort. In all six trials there was a very highly significant difference between acupuncture and usual care alone at 3 months ($p < 0.001$).



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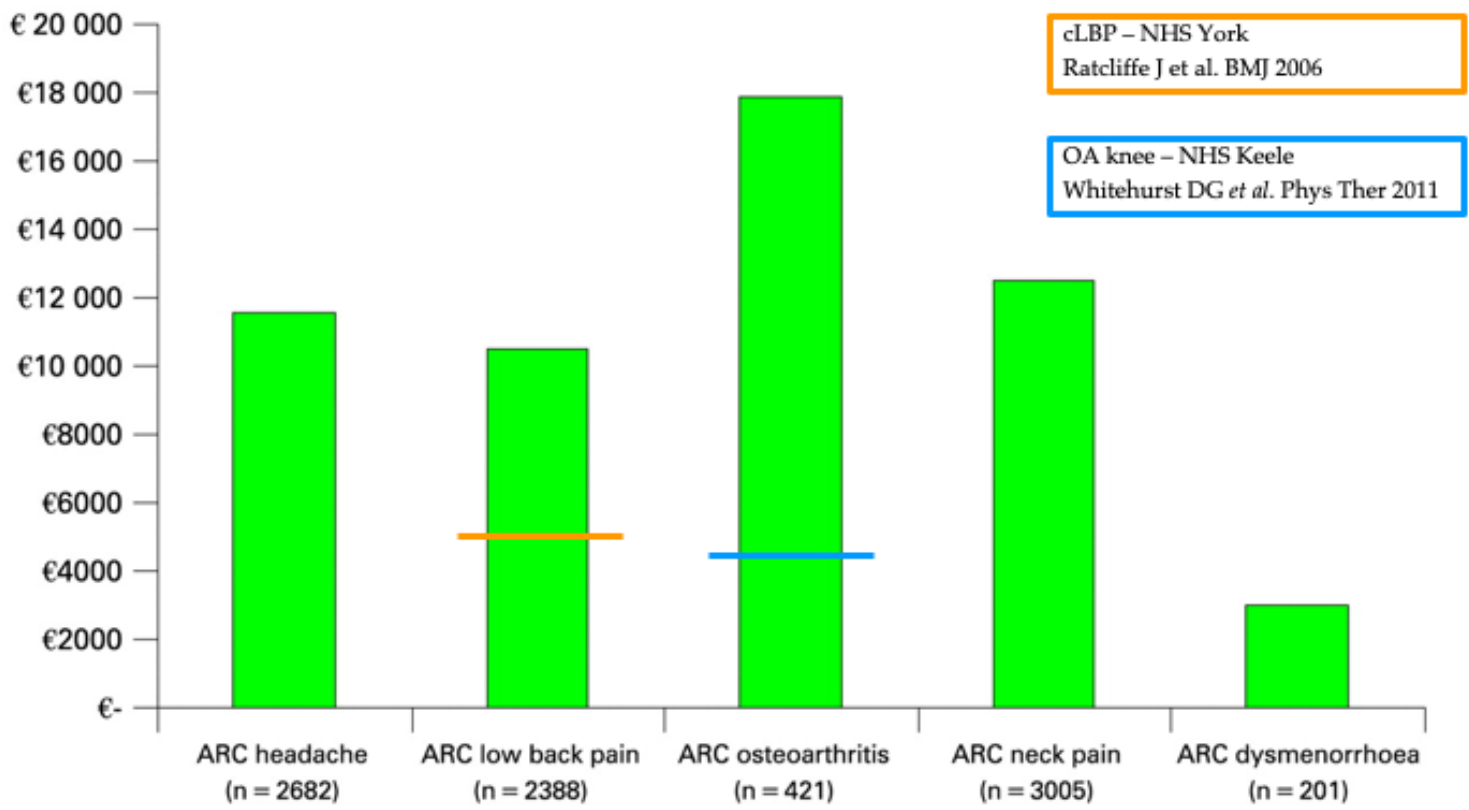
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ARC

The ARC studies were a series of large to very large pragmatic RCTs, with associated non-randomised cohorts. They used a standard design and included detailed economic analysis from a societal perspective. Subjects insured by one of the participating social health insurance funds were recruited by general practitioners across Germany for acupuncture treatment of either: osteoarthritis of the hip or knee; chronic neck pain; chronic low back pain; chronic headache; dysmenorrhoea; allergic rhinitis; or asthma (awaiting publication). If they agreed to be randomised, they either received 15 sessions of manual acupuncture over three months, or they waited three months for acupuncture treatment. If they expressed a strong preference for acupuncture and declined to be randomised, they received acupuncture treatment immediately. There was no standardisation of treatment, but only manual acupuncture was allowed.

Outcomes were measured at three and six months. After three months the group randomised to usual care alone were given acupuncture treatment. The primary outcomes were all set at three months. ARC chronic headache used the reduction in days with headache per month. ARC low back pain measured back function assessed by the HFAQ. ARC osteoarthritis used the change in WOMAC score, and ARC chronic neck pain used a validated neck pain and disability scale (NPAD). In ARC dysmenorrhoea the main outcome was the average pain intensity during the last menstruation before assessment measured on a numeric rating scale. ARC allergic rhinitis used the Rhinitis Quality of Life Questionnaire (RQLQ).

Figure 4 This figure illustrates the cost utility of acupuncture in various conditions, expressed as a cost per quality-adjusted life-year gained at 3 months from baseline, compared with usual care alone. The data are derived from within the Acupuncture in Routine Care (ARC) trials, and represent societal costs (see text under methods).



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ARC

As part of the ARC programme of studies, additional measurements were performed to assess quality of life (QoL), costs and the cost effectiveness relationship of routine care plus acupuncture compared with routine care alone. QoL was assessed with the Short Form (SF)-36 questionnaire, using the subscales and the components scales. The SF-36 also served as the basic benefit estimator for the cost effectiveness analyses. At baseline and at three months the patients completed questionnaires which assessed the quality of life over the previous seven days. The costs considered were measured in societal perspective and included the direct healthcare related costs of acupuncture (cost of each acupuncture session was €35), physician visits and hospital stays, and any drugs prescribed. In addition to health insurance costs, the indirect costs caused by lost workdays were also taken into account. These were estimated to be approximately €78 per lost workday. Additional analyses were performed to estimate cost utility in the case of higher costs and better medical outcome. QoL measures using SF-36 were converted to quality adjusted life years (QALY), and the excess cost in the acupuncture group in each study was divided by the increment in QALYs gained in the acupuncture group compared with the usual care group. This gave an incremental cost effectiveness ratio (ICER) expressed as a cost per additional QALY.

The additional information here is from two trials carried out in the UK. These calculated direct costs to the NHS only, whereas the ARC trials reported societal costs, which included costs related to working days lost.

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The Acupuncture Trialists' Collaboration performed the first individual patient data meta-analysis (IDPM) of chronic pain trials, which was finally published in 2012 after being rejected by 4 or 5 general journals without significant negative peer review. This meta-analysis included individual data on 17 922 patients, from 29 trials, and clearly demonstrated efficacy of acupuncture over sham in chronic pain, and effectiveness over non-acupuncture controls.

A further analysis of this data with meta-regression attempted to define the characteristics of treatment associated with better or worse outcomes. Better outcomes were observed when more needles were used when acupuncture was compared with non-acupuncture controls. A sensitivity analysis (excluding three outlying RCTs with very much larger effect sizes than the others) showed that trials allowing electrical stimulation had a significantly stronger effect of acupuncture compared with sham and those with a longer average treatment session duration had a smaller effect compared to sham.

The patient level analysis showed a small but highly significant association between better outcomes and a higher number of treatment sessions.

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The latest version of the Acupuncture Trialists' Collaboration IPDM reports data on 20 827 patients from 39 trials. Many of the results in terms of effect size are similar to the original IPDM and a clear dose effect is seen when comparing acupuncture to no acupuncture controls in terms of the number of sessions.

This update also has sufficient data to demonstrate a significant difference in the effect size of acupuncture over sham acupuncture when penetrating as opposed to non-penetrating sham is used as a control. As might be expected the effect of acupuncture appears larger when compared with controls that do not pierce the skin.

A word of caution here though. It appears that the use of sham devices may reduce the effect of both acupuncture and sham acupuncture, even though the difference between them may be larger than that between acupuncture and penetrating shams. So there may be a nocebo element from the use of these rather artificial devices used to support non-penetrating needles.

Table 2
Primary Analyses (N = 44 Trials)

Analysis	Indication	Sham				No Acupuncture Control			
		Studies, n	FE (95% CI)	Heterogeneity P	RE (95% CI)	Studies, n	FE (95% CI)	Heterogeneity P	RE (95% CI)
Main analysis	Nonspecific musculoskeletal pain	10	.30 (.21-.38)	< .001	-.49 (.16-.81)	12	-.54 (.50-.57)	< .001	.50 (.38-.63)
	Osteoarthritis	9	.24 (.17-.31)	< .001	-.45 (.15-.75)	10	.63 (.56-.69)	< .001	.74 (.46-1.01)
	Chronic headache	5	.16 (.08-.25)	.4	.16 (.08-.25)	7	-.44 (.39-.48)	< .001	-.56 (.35-.76)
	Shoulder	4	.57 (.44-.69)	.4	-.57 (.44-.69)	0	No trials		

Table 3
Sensitivity Analyses Including Only Pain End Points Measured Between 2 and 3 Months After Randomization

Analysis	Indication	Sham				No Acupuncture Control			
		Studies, n	FE (95% CI)	Heterogeneity P	RE (95% CI)	Studies, n	FE (95% CI)	Heterogeneity P	RE (95% CI)
Main analysis	Nonspecific musculoskeletal pain	5	.13 (.01-.25)	.005	.23 (-.03 to .49)	9	.60 (.56-.64)	< .0001	-.47 (.34-.61)
	Osteoarthritis	7	.31 (.23-.39)	< .0001	.69 (.24-1.14)	9	.73 (.66-.80)	< .0001	.88 (.61-1.15)
	Chronic headache	5	.14 (.06-.22)	.4	.14 (.06-.22)	7	-.43 (.38-.47)	< .0001	-.45 (.27-.63)
	Shoulder	2	No meta-analysis						

Abbreviations: FE, fixed effects estimate; RE, random effects estimate.

In summary, the effect of acupuncture over sham acupuncture in chronic pain is about 0.2 SMD (standardised mean difference: mean difference divided by standard deviation – referred to here as effect size), and the effect of acupuncture over no acupuncture controls is about 0.5 SMD. An effect size of 0.2 is small, but 0.5 is moderately large and very likely to be of clinical relevance. There is no practical point in assessing clinical relevance over a sham intervention, since the latter is not an option in practice; however, unfortunately the main guideline producer in the UK (NICE) insists on measuring the clinical relevance of acupuncture compared with sham acupuncture and not usual care (no acupuncture) controls.

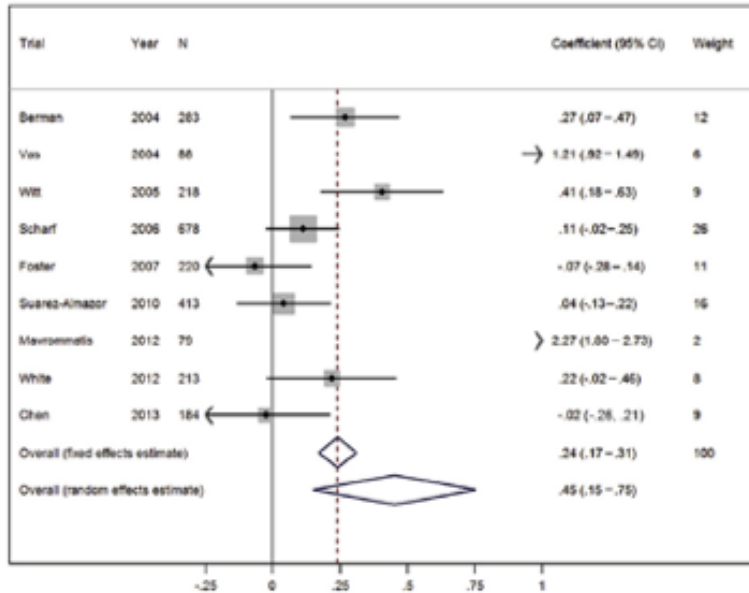
There are often arguments over whether fixed effects or random effects should be used. These are two methods of pooling data – similar methods with different assumptions. The fixed effect method assumes that the test intervention is better than control, and the random effects method does not make this assumption. I prefer fixed effects for acupuncture versus sham but I am not so clear that this is better when comparing acupuncture with no acupuncture controls, some of which may include best conventional care. Note that the CIs (confidence intervals) are generally much wider with the random effects method.

Heterogeneity (variability) of the results is high in most of the analyses – reflected in the very low p values. This does not concern me when pooling acupuncture data. Normally it would reduce the level of certainty in a result, but in the case of acupuncture trials we know that there is considerable clinical heterogeneity in the way acupuncture and sham acupuncture is applied, so statistical heterogeneity is not a surprise.

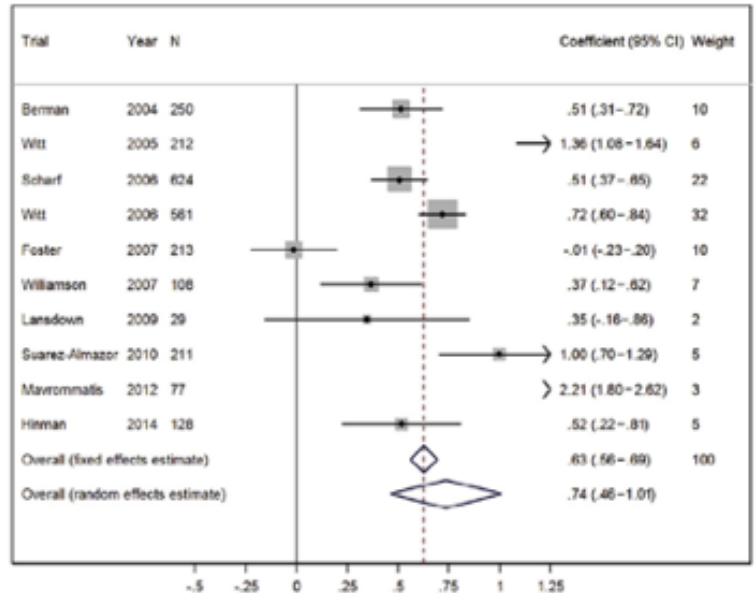
acupuncture vs sham

acupuncture vs no acupuncture

Osteoarthritis



Osteoarthritis



goo.gl/6XQeXv

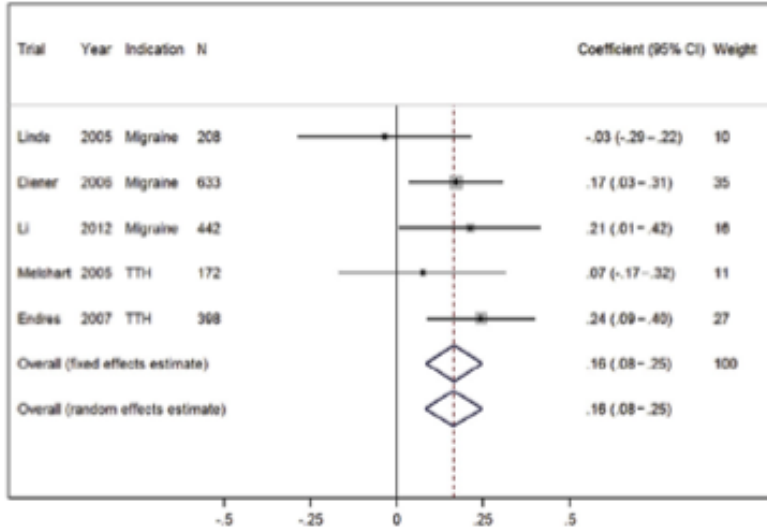
The forest plot on the left shows a small but highly significant effect of acupuncture over sham. The analysis is dominated by Scharf 2006 – one of the three arm comparative GERAC trials. Directly above it in the plot is the ART trial (Witt 2005). Go back to the slides summarising the ART and GERAC trials and compare the results in the acupuncture and sham acupuncture groups. You will see that the responder rate for acupuncture is similar, but there is a very big difference in the result of the sham group. Why such a difference? Well the ART studies were more tightly controlled and involved fewer centres (28 versus 315 in GERAC). All the practitioners in the ART studies met and were instructed on correct application of the sham technique. In the GERAC trial the practitioners received written instructions only.

The forest plot on the right shows a moderately large and highly significant effect of acupuncture over no acupuncture controls. The biggest influence this time is from the ARC trial (Witt 2006 – note this is not the same as the ART trial: Witt 2005). This trial compared acupuncture with a waiting list made up of patients who agreed to defer the start of their treatment by 3 months. It probably gives the most useful measure of the effect of acupuncture in practice. The comparison above this is from the GERAC trial (Scharf 2006), and the results are quite similar, but in this case both groups received physical therapy sessions, and the no acupuncture group received normal doses of NSAIDs.

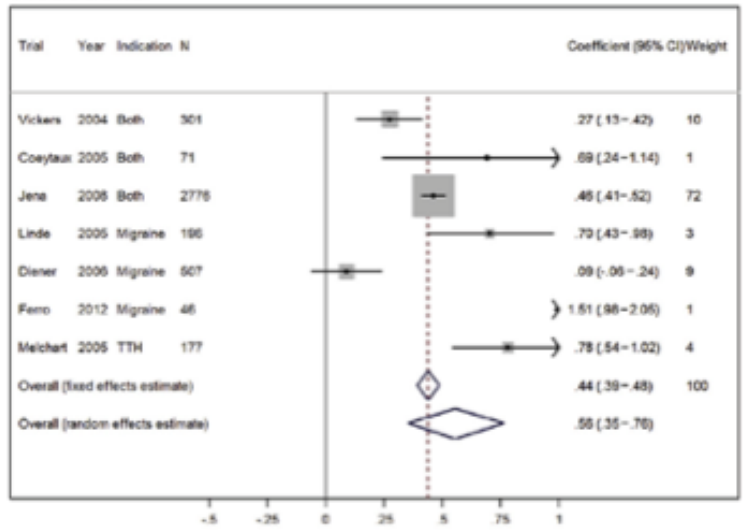
acupuncture vs sham

acupuncture vs no acupuncture

Headache



Headache



goo.gl/6XQeXv

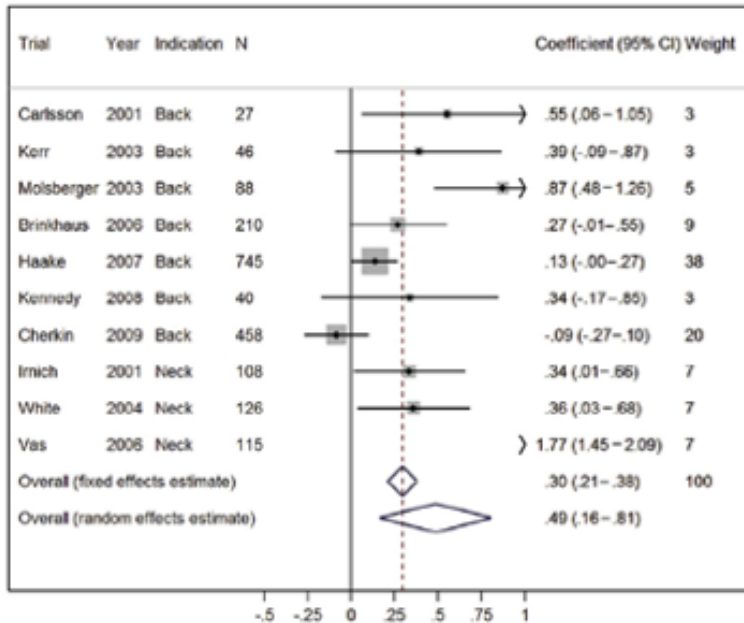
The forest plot on the left shows a very small but significant effect of acupuncture over sham. The first trial listed in this analysis is the ART migraine trial (Linde 2005). As you can see the point estimate is left of the line of no effect. This means that the sham group did marginally (not significantly) better than the true acupuncture group. If you look back to the ART summary slide you will see that the responder rate in the sham group was over 50% - probably the biggest surprise of the ART studies.

The forest plot on the right shows a moderately large and highly significant effect of acupuncture over no acupuncture controls. This plot is dominated by the ARC trial (Jena 2008) - it is given a 72% weighting in the analysis (this is based on size and narrow confidence intervals).

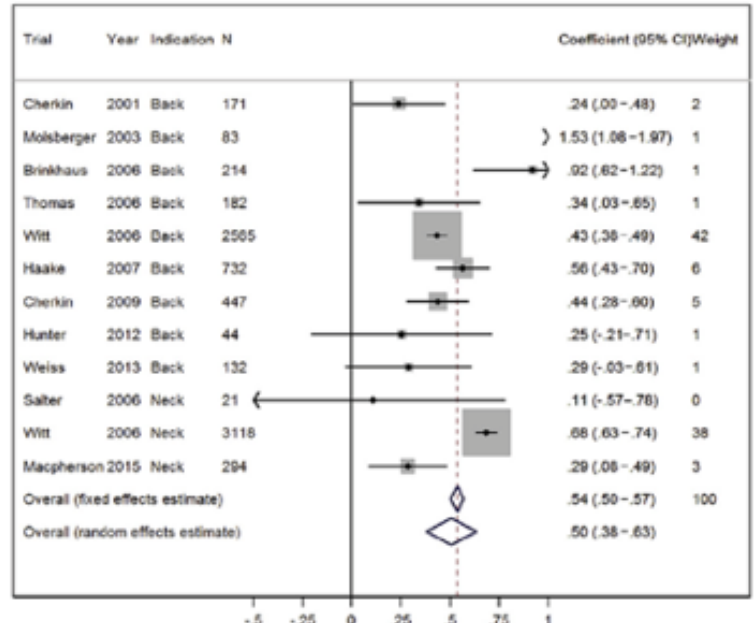
acupuncture vs sham

acupuncture vs no acupuncture

Musculoskeletal Pain



Musculoskeletal Pain



goo.gl/6XQeXv

The forest plot on the left shows a small but significant effect of acupuncture over sham in back and neck pain. This analysis is dominated by Haake 2007 (GERAC low back pain) and Cherkin 2009 (a 4-arm trial from the US in which all three acupuncture groups, including a cocktail stick sham, were twice as good as conventional care). If you look at the same two trials in the forest plot on the right, you will see moderately large effects over guideline-based conventional care, with results similar to the very large ARC trial (Witt (a) 2006). The difference reflects the moderately large effect of sham acupuncture in these trials. Data from the forest plot on the left has been used to create summary data that estimates the effect of acupuncture in back pain at 0.2 and the effect in neck pain at 0.8. This grossly exaggerates the real difference in effect, and the difference is dominated by different effects in the sham groups rather than the real acupuncture groups (see below). Note the very large effect measured in Vas 2006 in neck pain. The sham used in this trial was mock TENS. Note also a comment in the IPDM paper that the effect of acupuncture in neck pain appears to disappear faster than for other types of pain. This is entirely due to the change (gradual improvement) over time in the mock TENS group of Vas 2006. The effect of acupuncture in neck pain appears stable and similar to other forms of chronic pain assessed. This example illustrates the risk of only looking at intergroup differences in meta-analysis, and using small heterogeneous data sets.

The forest plot on the right shows a moderately large and highly significant effect of acupuncture over no acupuncture controls in back and neck pain. This analysis is dominated by the ARC trials (Witt (a) 2006 and Witt (b) 2006), and these give a more accurate, real world, picture of the difference in the effect of acupuncture in back pain and neck pain. There does appear to be a difference, with neck pain showing a slightly larger effect. Returning to the summary slide of the ARC trial results will reveal a larger percentage change in the primary outcome measure in back pain than neck pain in both real and control groups, but a bigger difference in neck pain. These trials used different outcome measures, so in this case it is safer to look at the difference over control.

Table 6. Results of Univariate Metaregression Analyses for the Effect of Acupuncture Characteristics on Acupuncture Effect

CHARACTERISTIC	SHAM ACUPUNCTURE				NO ACUPUNCTURE CONTROL			
	TRIALS, N	B	95% CI	P	TRIALS, N	B	95% CI	P
Style of acupuncture	25				25			
Some TCM versus Western only		-.00	-.49 to .48	>.9		.10	-.55 to .74	.8
TCM only versus some Western		.02	-.38 to .42	.9		-.07	-.42 to .28	.7
Point prescription	25				25			
Fixed needle formula		Reference		.6		Reference		.075
Flexible formula		.20	-.21 to .60			.01	-.45 to .46	
Fully individualized		-.01	-.75 to .73			-.34	-.79 to .10	
Electrical stimulation allowed	25	.32	-.11 to .75	.14	25	-.12	-.50 to .26	.5
Manual stimulation allowed	25	.26	-.42 to .95	.5	25	-.38	-.99 to .23	.2
Moxibustion allowed		No trials allowed			25	-.32	-.71, .06	.10
Other adjunctive treatment allowed	25	-.04	-1.00 to .92	.9	25	-.22	-.59 to .16	.3
De qi attempted	25	.29	-.67 to 1.24	.6	21	.74	-.04 to 1.52	.063
Acupuncture-specific patient practitioner interactions allowed	25	-.03	-.50 to .44	.9	25	-.05	-.38 to .28	.8
Minimum years of experience required	25	.04	-.05 to .13	.4	25	.05	-.03 to .12	.2
Maximum number of sessions (per 5 sessions)	25	-.01	-.23 to .22	.9	25	.01	-.12 to .14	.9
Patient-level analysis	5 (1,317/1,377)	.09	-.31 to .48	.7	5 (8,036/10,157)	.10	-.01 to .21	.001
Patient-level analysis, including Hinman et al ³⁹	6 (1,421/1,517)	-.03	-.36 to -.30	.9				
Frequency of sessions (per week)	25	-.06	-.29 to .18	.6	25	.21	-.22 to .64	.3
Duration of sessions (per 5 minutes)	25	.06	-.13 to .25	.5	20	-.06	-.25 to .13	.5
Patient-level analysis	6 (2,863/2,969)	.01	-.08 to .09	.9				
Number of needles used (per 5 needles)	25	.05	-.17 to .27	.6	19	.16	-.05 to .38	.13
Patient-level analysis	5 (2,232/2,317)	.04	-.08 to .16	.5				
Age of practitioner (per 5 years)								
Patient-level analysis					6 (9,127/10,550)	-.01	-.04 to .02	.5
Male practitioner								
Patient-level analysis					6 (9,384/10,550)	-.07	-.16 to .02	.084

Abbreviation: TCM, traditional Chinese medicine.

NOTE: β is an estimate of the change in the effect of acupuncture in terms of standardized difference compared with controls for each characteristic; a positive β indicates a larger effect of acupuncture compared with controls for trials. The number of patients in the analysis and number of patients in included trials are given in parentheses where applicable.

In terms of the characteristics of acupuncture, the only factor that had a clear influence was the number of treatments, and this was only apparent in the comparison against no acupuncture. This perhaps does not come as a surprise, but it does suggest that we should be more focussed on providing enough treatment sessions and not worrying as much about other aspects of the acupuncture approach.

In this update the effect based on number of needles used was no longer significant, but a positive trend remained.

I have a particular interest in electroacupuncture (EA), so I am keen to highlight the fact that in the more mechanistic comparison of acupuncture over sham the use of EA as a treatment characteristic had the largest effect size (0.32) and the lowest p value (p=0.14) of any characteristic studied. This does not reach the commonly adopted level of statistical probability, but equates to a 6:7 chance of being a real effect.

Going back to the more pragmatic comparison of acupuncture over no acupuncture, there are a couple of interesting trends apparent. The largest was for 'de qi attempted', and this reached 0.74 with p=0.063. This might also suggest a dose effect, but strangely the characteristic 'manual stimulation allowed' actually had a moderately negative effect.

Another characteristic that approached significance in the pragmatic comparison was 'male practitioner' at a p value of p=0.084. The effect size associated with this was very small and negative at -0.07, but it is tempting to view this against a backdrop of mechanistic research on placebo in pain, and suggest that male practitioners might think about channelling their more feminine sides during consultations.

Acupuncture in Chronic Pain

Topics

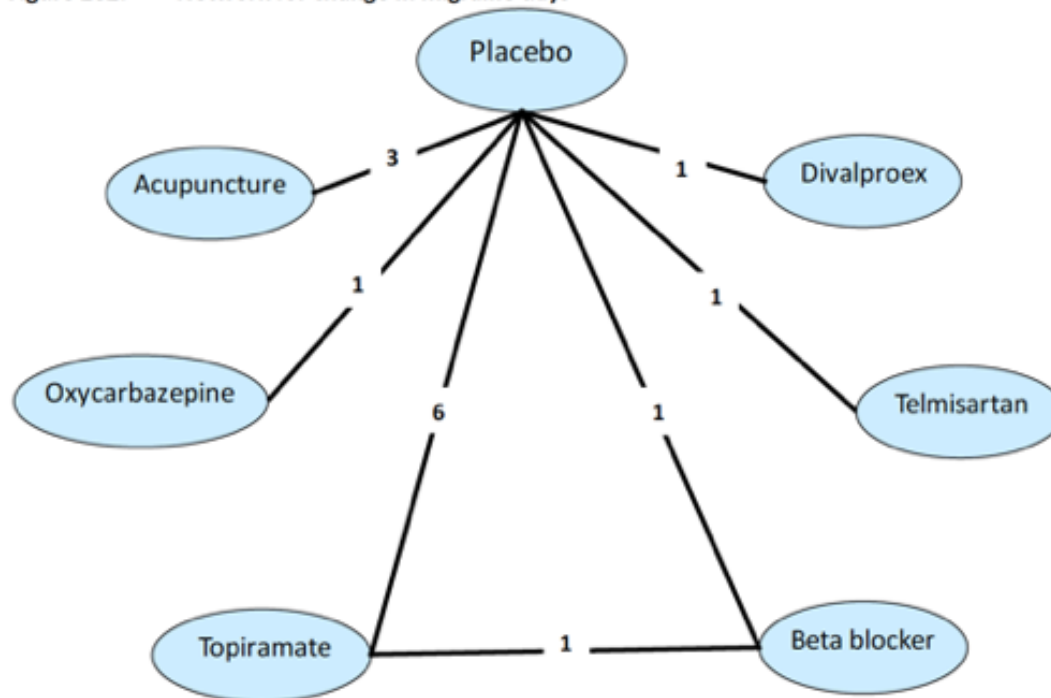
- ❖ What is sham acupuncture and why use it?
- ❖ the Modellvorhaben Akupunktur
- ❖ Vickers IPDM 2012
- ❖ Vickers IPDM update 2017
- ❖ NICE CG150 NMA 2012 – fast and dirty ←
- ❖ Corbett et al NMA 2013 – a proper NMA
- ❖ Saramago et al NMA 2016 – no sham in HRQoL
- ❖ Conclusions

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K.3 Results

A total of 12 studies from the original evidence review met the inclusion criteria for the network. Figure 282 shows the network created by eligible comparisons for the NMA, with numbers on the connecting lines indicating the number of studies for each comparison.

Figure 282: Network for change in migraine days



The trial data from the 12 studies included in the NMA for change in migraine days are shown in Table 24.

Network meta-analysis (NMA) is a method for combining data from multiple two-way comparisons of interventions so that both direct and indirect comparisons between interventions can be performed. For indirect comparisons there must be a common node (or intervention). In CG150 a limited network meta-analysis used placebo as a common node to compare acupuncture directly with topiramate, and concluded that topiramate was twice as good as acupuncture.

Note that there are only 12 studies included in this NMA.

Chart produced by Adrian White from data in CG150

White A, Cummings M. Inconsistent placebo effects in NICE's network analysis. *Acupunct Med* 2012;30(4):364-5.

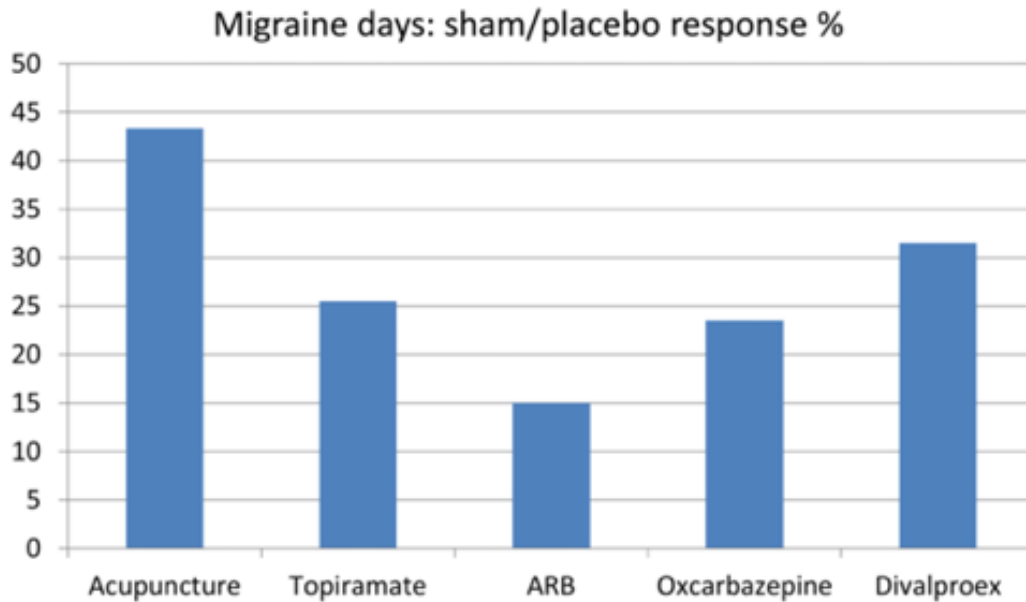


Figure 1 Migraine days: response rates of sham/placebo groups. ARB, angiotension receptor blocker.

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For this to be a valid analysis, sham acupuncture would have had to be the same as placebo topiramate, yet the absolute data (see above) seemed to indicate that sham acupuncture was associated with a higher responder rate than any other placebo included.

Chart produced by Adrian White from data in CG150

- modified by MC to include an estimate of the efficacy of topiramate & real acupuncture

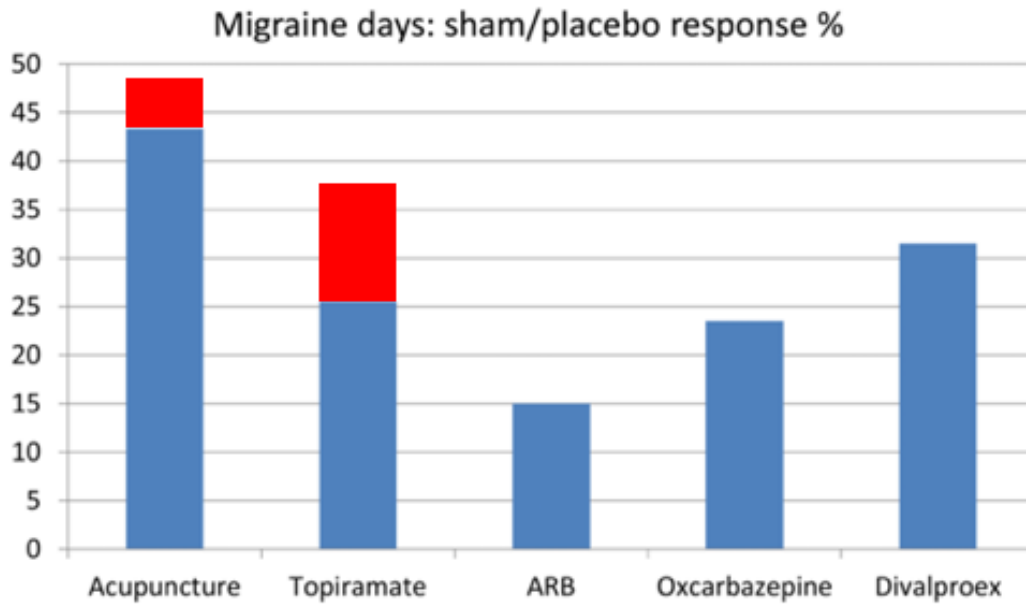


Figure 1 Migraine days: response rates of sham/placebo groups. ARB, angiotension receptor blocker.

In this chart, the effect of acupuncture and topiramate over their respective shams is included, and this reveals why NICE concluded that topiramate was twice as good as acupuncture (compare the height of just the red portions) whereas a different view seems to imply that sham acupuncture is superior to real topiramate.

Acupuncture in Chronic Pain

Topics

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- ❖ Conclusions

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Acupuncture and other physical treatments for the relief of pain due to osteoarthritis of the knee: network meta-analysis[☆]



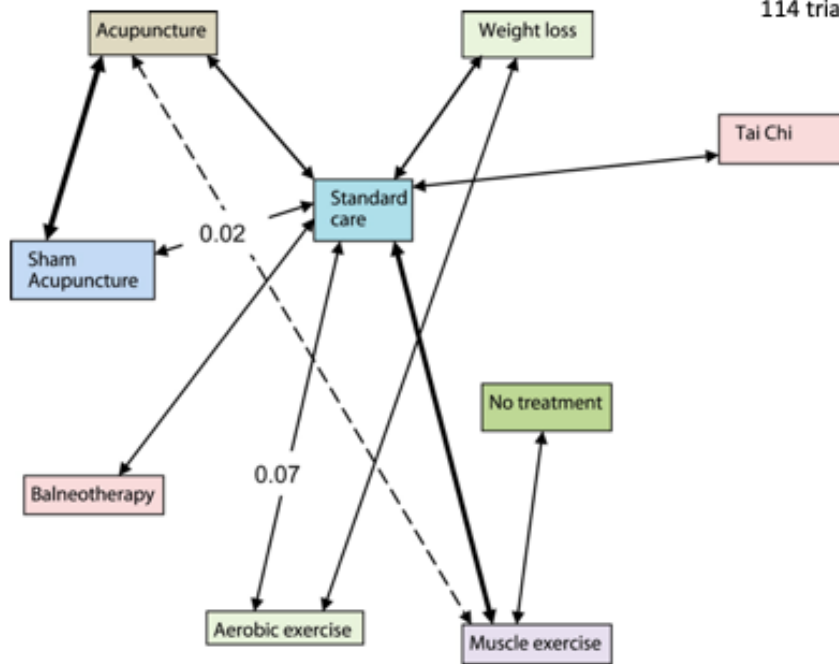
M.S. Corbett †*, S.J.C. Rice †, V. Madurasinghe †[‡], R. Slack †, D.A. Fayer †, M. Harden †, A.J. Sutton †, H. MacPherson †, N.F. Woolcott †

† University of York, UK
‡ University of Leicester, UK

Osteoarthritis and Cartilage 21 (2013) 1290–1298

114 trials, 22 treatments, 9709 patients

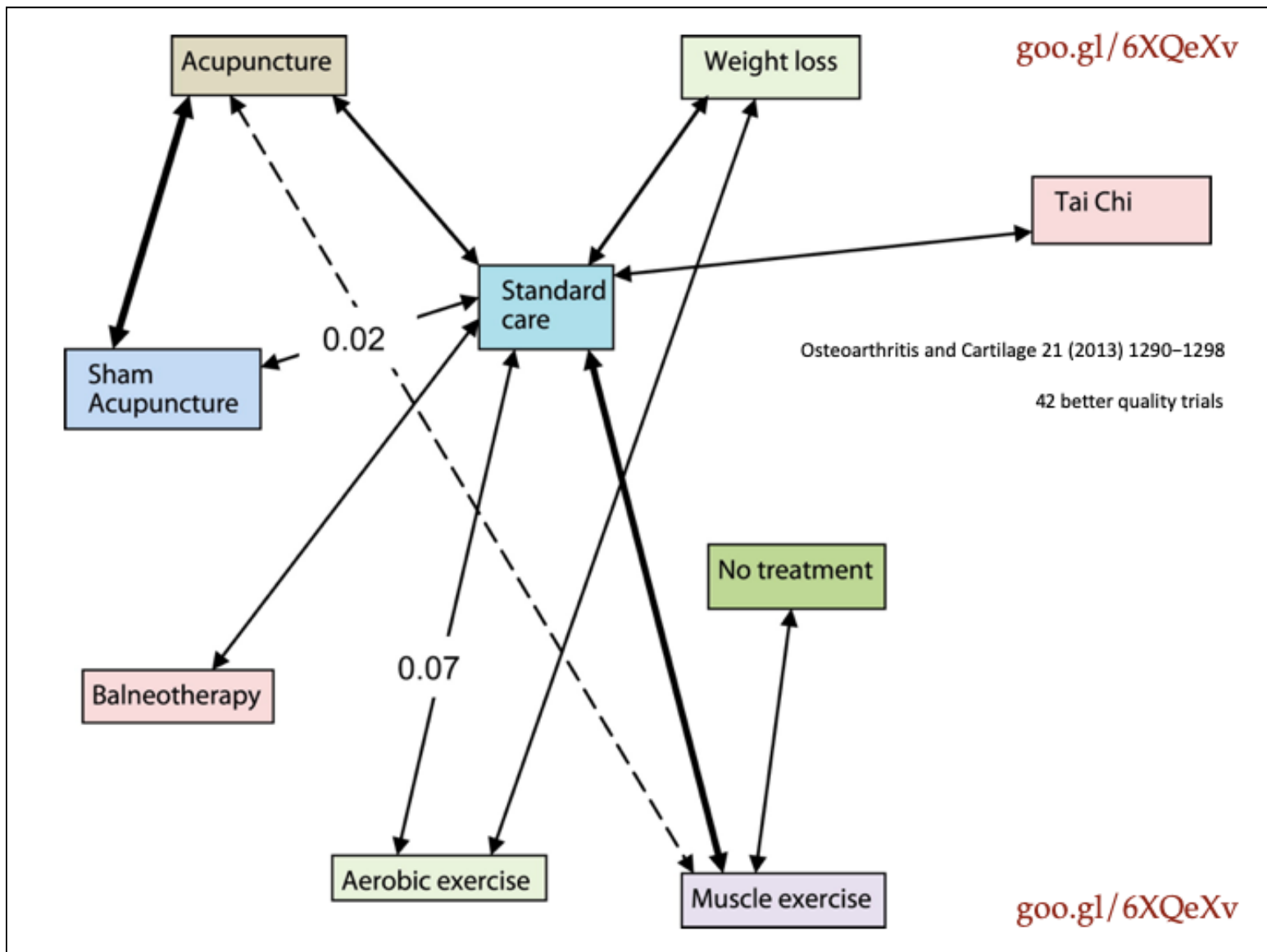
42 better quality trials



goo.gl/6XQeXv

This is a proper NMA, and the first performed including acupuncture. It was performed in a very well respected centre – the Centre for Reviews and Dissemination (CRD), York.

CRD is a research department that specialises in evidence synthesis, assembling and analysing data from multiple research studies to generate policy relevant research. We undertake high quality systematic reviews and associated economic evaluations, develop underpinning methods, and promote and facilitate the use of research evidence in decision-making.



Network diagram for the end of treatment analysis of better-quality trials. Each solid arrow indicates that there is a data point for that comparison entered into the analysis. The thickness reflects the number of trials. The dotted line reflects an extra comparison in a multi-arm trial. The numbers are a measure of inconsistency: 0 is no inconsistency; 1 is complete inconsistency.

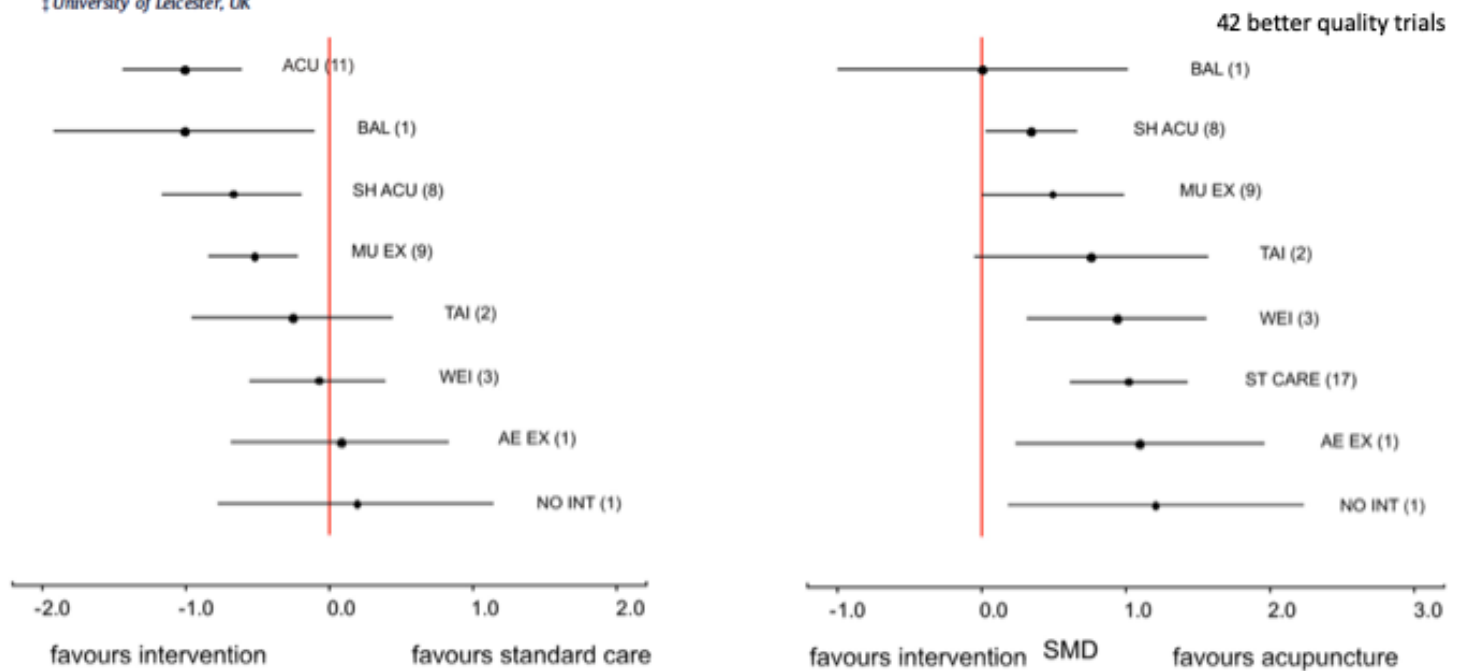
Acupuncture and other physical treatments for the relief of pain due to osteoarthritis of the knee: network meta-analysis[☆]



M.S. Corbett †*, S.J.C. Rice †, V. Madurasinghe †[‡], R. Slack †, D.A. Fayter †, M. Harden †, A.J. Sutton †, H. MacPherson †, N.F. Woolacott †

† University of York, UK
‡ University of Leicester, UK

Osteoarthritis and Cartilage 21 (2013) 1290–1298



Conclusions: As a summary of the current available research, the network meta-analysis results indicate that acupuncture can be considered as one of the more effective physical treatments for alleviating osteoarthritis knee pain in the short-term. However, much of the evidence in this area of research is of poor quality, meaning there is uncertainty about the efficacy of many physical treatments.

Acupuncture in Chronic Pain

Topics

- ❖ What is sham acupuncture and why use it?
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- ❖ Conclusions

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RESEARCH ARTICLE

Open Access



Methods for network meta-analysis of continuous outcomes using individual patient data: a case study in acupuncture for chronic pain

Pedro Saramago^{1*}, Beth Woods¹, Helen Weatherly¹, Andrea Manca¹, Mark Sculpher¹, Kamran Khan², Andrew J. Vickers³ and Hugh MacPherson⁴

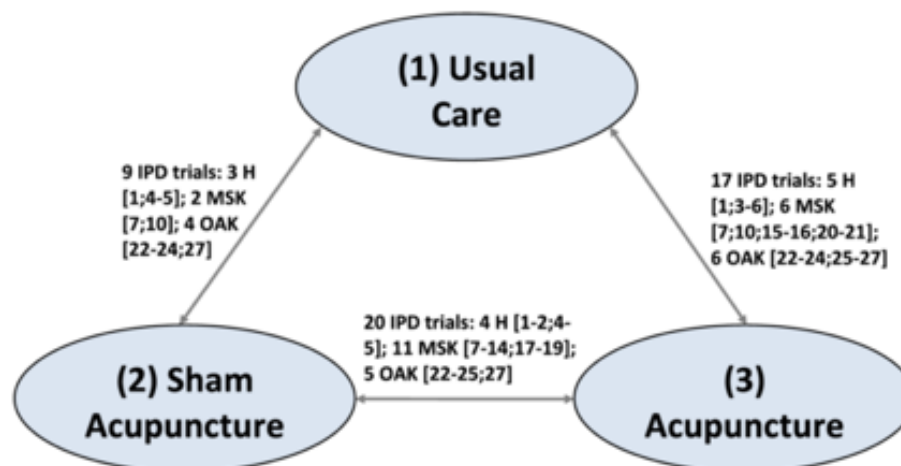


Fig. 1 Network of RCTs. Legend: In the network, a unique treatment category is indicated by a circle. Arrows between circles indicate that these treatments have been compared in a trial (trials are identified using 'I', numbered according to column 'ID' in Table 1). (Pain groups: H – Headache/migraine; MSK – Musculoskeletal; OAK – Osteoarthritis of the knee)

Data from the Acupuncture Trialists' Collaboration IPDM has been used in the first network meta-analysis using analysis of covariance in a continuous variable (VAS pain). Whilst this was not the intention of the paper, it has given us, for the first time, a large data set comparing sham acupuncture with usual care or best standard care (depending on the individual trial).

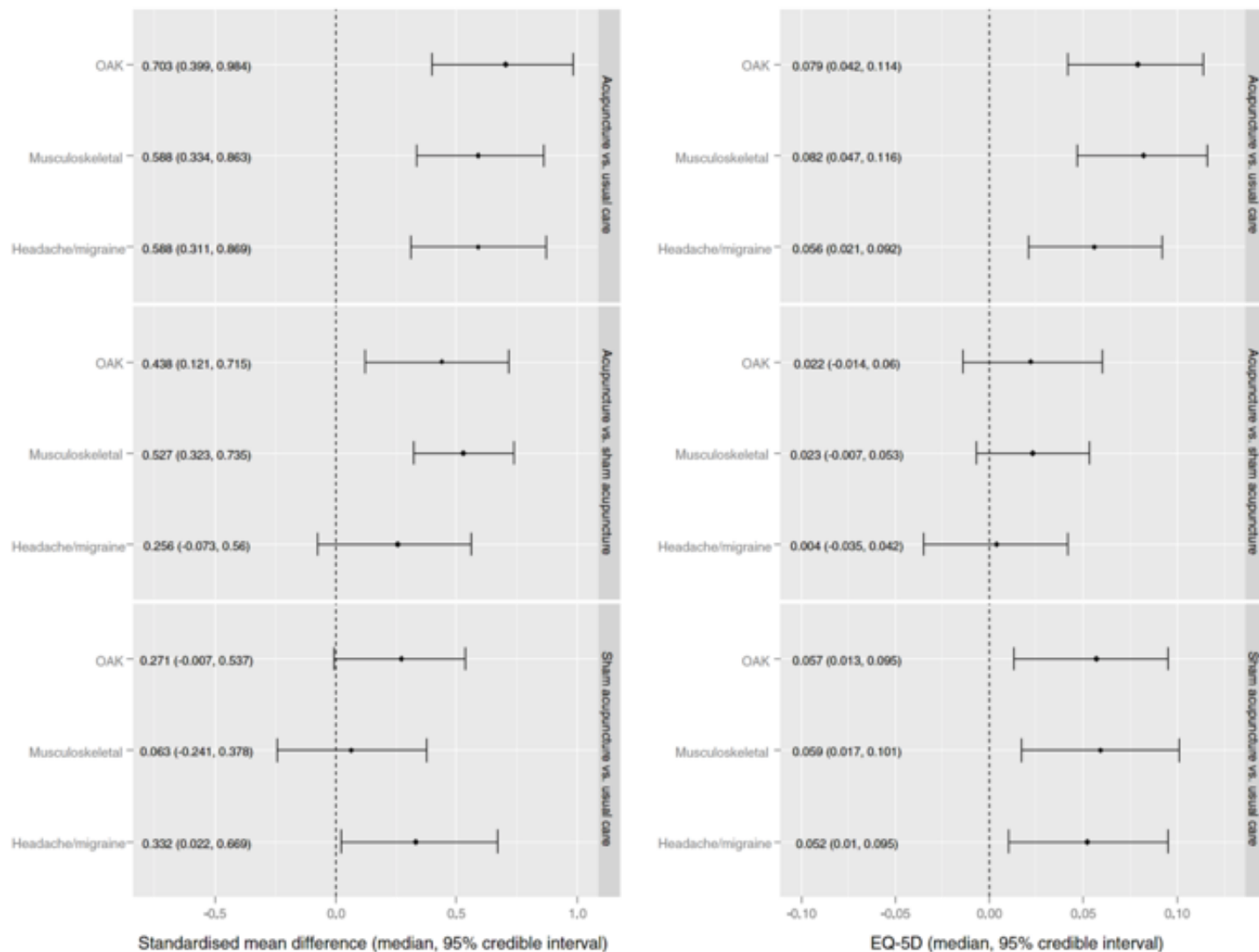


Fig. 2 Forest plot showing network meta-analysis results for standardised pain and EQ-5D outcomes

It is most interesting to note that sham is significantly superior to usual care in all conditions tested for health-related quality of life (HRQoL), and whilst acupuncture is superior to sham for pain outcomes, it is not superior in terms of HRQoL. This data must add to the weight of evidence that suggests sham acupuncture is far from being a placebo.

Note 1:

Usual care is a term used in the paper by Saramago *et al*, and it refers to the same data set labeled by Vickers *et al* as no acupuncture controls. This group includes a variety of interventions that could be described as standard or conventional care. Some involved quite intense treatment regimes, and others could be seen as more of a background usual care that might be common to all groups (ie including acupuncture and sham acupuncture groups).

Note 2:

Sham acupuncture mostly involves needling superficial tissues and has similarities with gentle forms of acupuncture. Non-penetrating sham or 'placebo' needles are blunt ended, and often cause significant discomfort and can penetrate the skin. It seems clear that sham acupuncture is not synonymous with the term 'placebo'.

Acupuncture in Chronic Pain

Topics

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- ❖ Saramago et al NMA 2016 – no sham in HRQoL
- ❖ Conclusions ←

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Problems with Sham Acupuncture?

- The comparison of acupuncture with sham acupuncture:
 - ◇ underestimates the effect of real acupuncture over 'placebo' control
 - because sham is not inactive
 - so acupuncture appears effective in practice but not in blinded RCTs
 - ◇ some sham devices may reduce the effect of real acupuncture
 - because they restrict the needling depth or stimulus
 - ◇ sham acupuncture can outperforms conventional medicine
 - see Haake *et al* (slide 10)
 - sham was 50% better than guideline-based conventional care in LBP
 - this varies with the degree to which sham is an active intervention
 - ◇ sham acupuncture outperforms usual care comparisons in HRQoL
 - a chance finding of Saramago *et al* 2016, but statistically robust

Acupuncture in Chronic Pain



The problem with Sham Acupuncture



Thank you for listening

Dr Mike Cummings
Medical Director BMAS

To find me **type BMAS** into **Google**



FaceBook: Mike Cummings
Twitter: @drmike001
LinkedIn: Mike Cummings
Google+: Mike Cummings
Biography: goo.gl/6XQeXv