# Evidence for acupuncture

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## Acupuncture mechanisms

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## Acupuncture in experimental pain

### – comprehensive reviews

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## Evidence for acupuncture relevant to primary care

### Chronic low back pain

A Cochrane review by Furlan *et al* of acupuncture and dry needling for low back pain in 2005, which included 35 RCTs, concluded that 'for chronic low back pain, acupuncture is more effective for pain relief and functional improvement than no treatment or sham treatment immediately after treatment and in the short term only'. [1] A systematic review (SR) published in the same year by Manheimer *et al* also found acupuncture to be significantly more effective than sham acupuncture in chronic low back pain.[2]

Subsequent to these reviews there have been a number of relevant studies published. The ART (**A**cupuncture **R**andomised **T**rial) study (n=298) from the Charité University Medical Centre in Berlin of acupuncture for chronic low back pain shows a trend in favour of verum over minimal (superficial non-point) acupuncture, but a significant difference between verum and the no (additional) treatment control group.[3] The standard deviation in the primary outcome measure in this trial exceeded the estimate in the sample size calculation by 50%, which reduced the intended statistical power of the trial considerably.

Thomas *et al* reported positive results in their pragmatic trial of acupuncture in chronic low back pain in primary care (n=241). They demonstrated effectiveness and cost-utility at 24 months – the cost per additional QALY was £4241.[4,5] The primary outcome for additional acupuncture over routine GP care was significant at 24 months but not at 12 months. This is a surprising result following a short course of acupuncture, since the prior systematic reviews demonstrated a short term effect only.[1,2]

The results of the very large pragmatic

ARC (**A**cupuncture in **R**outine **C**are) study on chronic low back pain (n=3093 randomised; 11 630 total cohort) confirm effectiveness and cost effectiveness of acupuncture, with the cost per additional QALY of €10 526.[6]

The GERAC (**Ger**man **Ac**upuncture trial) trial on low back pain (n=1162)[7] found acupuncture and minimal (sham) acupuncture to be superior to guideline-based standard treatment; however, acupuncture was not statistically superior to minimal (superficial non-point) acupuncture. On the basis of this, the German health authorities decided that acupuncture would not be included in routine reimbursement by social health insurance funds for the treatment of low back pain. One of the key findings in this trial was that the minimal (sham) acupuncture (often viewed as a 'placebo' control) was superior to guideline-based standard care (50% better in the primary outcome measure). This calls into question the validity of making judgements about the clinical relevance of the difference between acupuncture and minimal (sham or 'placebo' control) acupuncture.

A large (n=638), four-arm sham controlled and comparative trial performed in the US demonstrated no difference between individualised acupuncture, standardised acupuncture or simulated acupuncture (using blunted cocktail sticks) on mechanical low back pain, but all three groups were more than twice as effective as usual care alone.[8]

An individual patient data meta-analysis (IPDM) reported by Vickers *et al* in 2012 (see below), [9] includes pooled data from 5 of the best quality trials of acupuncture in low back pain in a sensitivity analysis. This includes data from the ART & GERAC trials described above,[3,7] but not the four-arm US trial.[8] Acupuncture was significantly superior to sham and to no acupuncture with pooled effect sizes of 0.20 and 0.46 respectively. An updated version of the IPDM reports similar effect sizes of 0.17 and 0.46 respectively.[10]

The NICE clinical guideline (CG88) for the early management of persistent non-specific low back pain (between 6 months and 1 year) included consideration of 12 sessions of acupuncture over 3 months.[11] Unfortunately the update of this guideline, titled 'Low back pain and sciatica',[12] published in November 2016 did not recommend acupuncture, as NICE began applying a minimal clinically important difference (MCID) as a new criterion to the difference of an intervention over sham or placebo. See the category 'NICE' on the BMAS blog at https://bmas.blog/ for comments on this change, and how it was selectively applied.

The decision not to recommend acupuncture for back pain in NG59 was rather controversial, because the evidence for acupuncture appeared to exceed that for many interventions that were recommended. The story of CG88 to NG59 is described in a presentation from the BMAS Spring meeting in the Paddington Hilton 2017.

It is disappointing to see the long awaited update of the Cochrane review adopt the MCID in the comparison of real acupuncture over sham as the primary indicator of efficacy.[13] This review, published in 2020, has been discussed on the BMAS Blog.

## Sciatica

There has been much less clinical research on sciatica than on chronic low back pain, although the two conditions are clearly related. Sciatica is often an excluded from trials of acupuncture in chronic low back pain, perhaps because the perceived prognosis is different.

In 2024, a moderately large (n=220) multicentre sham controlled trial with 2 parallel arms was carried out at 6 hospitals in China. The patient population were adults with unilateral sciatica from a herniated lumbar disc for at least 3 months. Their leg pain had to score 40 or more on VAS. Acupuncture or sham acupuncture was applied in 10 sessions over 4 weeks and the follow-up extended to 52 weeks. The active group improved significantly more than the sham and this difference was maintained at 52 weeks.[14]

A related but more severe condition – degenerative lumbar spine stenosis – was also investigated in 2024 via a multicentre

sham controlled trial in China. This time it was 5 hospitals but the size of the trial was comparable (n=196). Acupuncture performed 3 times a week for 6 weeks proved to be significantly better than a superficial needling control at the same points and the difference was maintained at 30 weeks.[15]

Another paper published in the same year has interesting and potentially relevant results, particularly to the big sciatica trial above. This one was a prospective cohort trial (n=90) looking at the rate of resorption of extruded disc material in patients with an acute disc prolapse and leg pain. An inflammatory preserving protocol was used, which included acupuncture and excluded the use of steroids or NSAIDs. The mean time to complete disc resorption was just 4.4 months.[16] This compares very favourably with the 6 to 12 months quoted in The Atlas of Sciatica.[17]

## Chronic headache

The first Cochrane review on acupuncture for idiopathic headache was tentatively positive.[18]

In a pragmatic trial in the UK, Vickers and Wonderling show definitive effectiveness and cost effectiveness – the cost per additional QALY was £9180.[19,20]

Efficacy was still in some doubt following the results of the German ART studies in migraine and TTH.[21,22] Responder rates were good for needling but the rates in the minimal (sham) needling groups were also high. Responder rates were confirmed in a large epidemiological study (n=2022).[23] The ARC study on headache confirmed effectiveness compared with usual care alone (n=3182 randomised; 15 056 total cohort),[24] and confirmed cost effective-ness (n=2682), with the cost per additional QALY of €11 590.[25]

The GERAC trial on migraine (n=960) showed that outcomes do not differ between acupuncture, minimal (sham) needling, and standard therapy (1st beta-blocker; 2nd flunarizine; 3rd valproic acid).[26] The responder rates at 26 weeks after randomisation were 47%, 39% and 40% respectively. When reanalysed in the IPDM by Vickers *et al*, the difference between acupuncture and minimal (sham) acupuncture became statistically significant.[9] The reason for this was that Vickers *et al* used a more powerful statistical method – ANCOVA.[27]

In 2009 the Cochrane review was updated and split into acupuncture for migraine prophylaxis,[28] and acupuncture for tension-type headache.[29] A significant effect over sham was noted in the latter but not the former. Acupuncture appeared to be at least as good (statistically superior) as prophylactic medication in migraine.

The NICE clinical guideline (CG150) on diagnosis and management of headaches in young people and adults recommended the use of acupuncture for prophylaxis of tension type headache and migraine,[30] although there is some debate over the network meta-analysis that showed acupuncture to be only half as good as topiramate,[31] when the same data seems to show that sham acupuncture is marginally better than real topiramate.

An update to CG150 was published in 2015, and in 2021, which only affected drug recommendations, and the recommendations for acupuncture remain.

The Cochrane reviews were updated in 2016,[32,33] and the conclusions remain positive. Data from the IDPM was used,[9] and for the first time acupuncture has been shown to be marginally superior to sham, as well as medication in migraine prophylaxis.

Since then, there have been some further clinical trials on migraine and TTH, and we have seen the emergence of monoclonal antibodies directed at CGRP (calcitonin gene-related peptide) and its receptors. The effect of these has not been directly measured against acupuncture; however, the RCT data suggests there is little difference and that the rate of side-effects is more than double with these rather expensive monoclonals.[34] See the BMAS Blog, and in particular the category on headache.

## Knee osteoarthritis (OA knee)

The largest sham controlled trial to date is the GERAC OA knee trial (n=1007).[35] This

trial used off-point superficial acupuncture in the sham, and a third arm of conservative treatment only (physiotherapy and NSAIDs). Both acupuncture groups (traditional Chinese acupuncture and sham acupuncture) were significantly better than conservative treatment alone. The improvement in WOMAC index in the real acupuncture group was very similar to that in the ART OA knee trial (around 20% reduction at 26 weeks).[36] The key difference between ART and GERAC appears to be the effect size in the minimal acupuncture group (it was markedly higher in the GERAC trial than in the ART trial) and this may reflect the degree of training in, and commitment to, the sham acupuncture procedure.

An SR by White *et al* included 13 RCTs. [37] The results from the five high quality trials (n=1334) were pooled in meta-analysis for the primary outcome, and demonstrated a significant effect of acupuncture versus sham in short term pain. A subsequent SR by Manheimer *et al* found very similar results in their meta-analysis,[38] although their interpretation differed in terms of clinical relevance.

The pragmatic ARC study on acupuncture for OA in the hip and knee (n=712 randomised; 3633 total cohort) demonstrated marked clinical improve-ment, which was maintained at six months, from a 15 session course of treatment.[39] The economic analysis performed alongside the ARC study (n=421) demonstrated cost effectiveness of €17 845 per additional QALY.[40] A further health economic assessment in the UK, that formed part of the APEX trial,[41] provided a more favourable figure of £3889 per additional QALY for an intervention including advice, exercise and acupuncture. [42]

The most recent Cochrane review of acupuncture for peripheral joint OA (led by Manheimer)[43] included 16 trials and 3498 participants. Twelve trials were on OA knee, three on OA hip and one included both. The authors concluded:

*Sham-controlled trials show statistically significant benefits; however, these benefits are small, do not meet our pre-defined thresholds for clinical relevance, and are probably due at least partially to placebo effects from incomplete blinding. Waiting list-controlled trials of acupuncture for peripheral joint osteoarthritis suggest statistically significant and clinically relevant benefits, much of which may be due to expectation or placebo effects.*

We (White & Cummings)[44] argue that you can only test the biological plausibility of acupuncture against sham acupuncture, not its clinical relevance, since sham is invariably an active comparator.

The NICE clinical guideline (CG59) on osteoarthritis recommended that electroacupuncture should not be used on the basis of the perceived cost derived from health economic modelling.[45] This guideline was much debated,[46–48] and an alternative economic analysis seemed to favour acupuncture;[49] however, the updated guideline (CG177) did not recommend acupuncture,[50] despite evidence of efficacy over sham, effectiveness and cost effectiveness within threshold. The difference beyond sham is the sticking point, and the wording of the Cochrane review above is repeated as the excuse. Acupuncture did not achieve a standardised mean difference (SMD) of 0.5 over sham acupuncture; however, few interventions if any in osteoarthritis do achieve this.

Further evidence that suggests acupuncture can play a useful role in osteoarthritis comes from a network meta-analysis (NMA).[51] This was a comprehensive NMA of physical treatments for pain relief in osteoarthritis of the knee (OA knee). A total of 114 trials including 22 different interventions in 9709 patients provided data suitable for NMA. The higher quality trials were of acupuncture (11 trials) and muscle strengthening exercises (9 trials). The latter is recommended in national clinical guidelines as a core treatment in OA knee.[45,50] Acupuncture was significantly better than muscle strengthening exercises with an effect size of 0.49 (SMD). This seems to raise questions about why acupuncture is not recommended as a treatment in OA.[48]

A further small but rigorous study published in JAMA again raised the question of MCID over sham.[48] There was a

significant difference for needle acupuncture over a no treatment control who were not aware of the trial (Zelen design), and therefore not disappointed. The paper has raised some debate over interpretation of the results.[53]

A moderately large trial (n=301) from Beijing and Hangzhou published in 2019 demonstrated the superiority of strong EA over weak EA or sham EA in OA knee.[54] The outcome used in this trial was conditioned pain modulation (CPM), measured using cold water immersion of the contralateral hand and a von Frey filament compression of a tender point on the affected knee. The nice thing about this study is that, as well as demonstrating a benefit of strong EA over the comparators it also provides data consistent with the purported mechanisms of symptom relief, that is enhanced descending inhibition of pain.

A further large (n=480) multicentre, 3 arm trial from China compared EA, MA and sham in OA knee.[55] Treatment was applied 3 times per week for 8 weeks, and EA was statistically superior to sham at 4, 8, 16 and 26 weeks. MA was statistically superior to sham at 16 and 26 weeks.

## Hip osteoarthritis (OA hip)

In 2018, a Cochrane review of acupuncture in hip OA (again led by Manheimer) was published for the first time.[56] It only contained data from 6 trials and 413 patients, so the neutral conclusion is justifiably uncertain.

There is little data on the technique found clinically to be most effective, that is periosteal needling of the greater trochanter, so there is a need for research in this area.

## Neck pain

The first SR of acupuncture for neck pain was neutral,[56] but this was based on relatively small trials with methodological drawbacks. The ARC study on neck pain (n=3766 randomised; 14 161 total cohort) clearly demonstrates effectiveness,[57] and combined with confirmed efficacy over sham for acupuncture in chronic low back pain [see above], it seems reasonable to postulate that there is also specific efficacy for acupuncture in neck pain. The economic analysis that formed part of the ARC study found the cost per additional QALY of acupuncture in chronic neck pain was €12 469.[59]

A Cochrane review was published in 2006,[60] although this does not include the ARC study above. It found moderate evidence that acupuncture relieves pain in chronic mechanical neck disorders. Interestingly the 10 trials included had a total of only 661 subjects – one fifth of the size of the randomised element of the ARC trial.[58]

An updated Cochrane review was published in 2016, but this has been withdrawn after comments on interpretation of the ARC trial data.

The latest version of the Vickers *et al* IPDM reports a rather large effect size of 0.83 for acupuncture over sham in neck pain.[10] So this, the largest pooled data set from controlled trials, puts the effect size in neck pain at around 4 times that in back pain. This is likely to be an exaggeration of the real difference due to two large sham controlled trials in chronic low back pain that demonstrated large effects in the sham acupuncture groups.[7,8] In these trials both real and sham acupuncture were substantially better than conventional care controls, but since the difference between real and sham forms of the intervention were small, this data artificially holds down the pooled effect size in meta-analyses, leading to the conclusion by some that acupuncture does not work.

## Shoulder pain

The Cochrane review on acupuncture for shoulder pain in 2005 was inconclusive but suggested that there may be a short term benefit on pain and function.[61] Since then there have been two interesting trials. Vas *et al* demonstrated the advantage of manual acupuncture to a single point (ST38) versus sham (mock TENS) along with physical therapy rehabilitation for shoulder pain in 425 subjects.[62] The GRASP trial (German

Randomized Acupuncture trial for chronic Shoulder Pain) tested acupuncture against a distant superficial off-point sham and conventional orthopaedic care in 424 subjects with chronic shoulder pain.[63] Acupuncture proved to be superior to sham and conventional orthopaedic care, although the dropout rate in the sham group was rather high at 45%.

The latest version of the Vickers *et al* IPDM reports a moderate effect size of 0.58 for acupuncture over sham in shoulder pain.[10] So this is theoretically large enough for a positive decision from NICE, but NICE do not have a guideline for shoulder pain as yet.

## Individual patient data meta-analysis

The Acupuncture Trialists' Collaboration performed the first individual patient data meta-analysis (IPDM) of chronic pain trials.[9] This meta-analysis included individual data on 17 922 patients, from 29 trials, and the results clearly demonstrated efficacy of acupuncture over sham in chronic pain, and clinically relevant 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.[64] 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.

Data from this IPDM was subsequently used in the first network meta-analysis using analysis of covariance in a continuous variable (VAS pain).[65] 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). It is most interesting to note that sham was 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. See the BMAS blog for further comments on this paper.

The latest version of the IPDM reported data on 20 827 patients from 39 trials.[10] Many of the results in terms of effect size are similar and a clear dose effect is seen when comparing acupuncture to no acupuncture controls. This update also had 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. The meta-regression on this larger data set only demonstrated the importance of the number of treatment sessions. Other factors such as the number of needles or methods of stimulation did not show any significant statistical influence on the results. See further comments on the BMAS blog.

## Chronic pain

NICE guideline NG193 considered evidence for acupuncture,[66] but excluded data on low back pain and osteoarthritis, because these had been included in other clinical guidelines.[12,45,50] This was beneficial to acupuncture by excluding the two large RCTs in chronic low back pain that demonstrated large effects in the sham acupuncture groups, and thus small differences between real and sham acupuncture.[7,8]

NG193 recommends a single course of acupuncture or dry needling for chronic primary pain. Stipulations were included regarding the time spent on the treatment course and the health professional grade so as to limit overall costs.

## Nausea & vomiting

This was the first area with a positive SR.[67] The best evidence is for post-operative nausea and vomiting (PONV), in which the NNT is estimated to be between 4 and 5 for early PONV.[68]

The latest Cochrane review on the subject concludes:[69]

*P6 acupoint stimulation prevented PONV. There was no reliable evidence for differences in risks of postoperative nausea or vomiting after P6 acupoint stimulation compared to antiemetic drugs.*

Despite repeatedly positive systematic reviews over a 25-year period, this technique has yet to be adopted universally.

## Overactive bladder

A trial of electroacupuncture (EA) to SP6, referred to by urologists as PTNS (percutaneous tibial nerve stimulation), has demonstrated efficacy of this intervention compared with sham (including the Streitberger needle) in 220 subjects with overactive bladder symptoms.[66] Other studies suggest that the technique compares favourably to the drug tolterodine,[70] and that it appears to be a viable long term therapy.[71]

It is interesting to note that PTNS was approved by NICE in 2010,[72] with an effect size that would not meet the requirement set out for acupuncture in terms of MCID.

## Chronic constipation

A huge trial on chronic severe functional constipation was published in mid 2016. It was a two-armed RCT with 1075 patients receiving 28 sessions of EA or sham over 8 weeks.[74] EA was performed to muscle points in rectus abdominis and manual acupuncture to a point in tibialis anterior. The sham was superficial off point and inactive EA. The real EA was significantly better, with effects that lasted throughout a 3-month follow-up period. So, the results were encouraging, although the frequency of treatment would be difficult to reproduce outside East Asia. See this BMAS blog.

Subsequently a large (n=560) non-inferiority trial from the same research group tested the same EA protocol at a similar frequency of treatment against the high affinity 5–HT4 agonist prucalopride.[75] EA proved to be non-inferior, and the results were actually compatible with equivalence. The EA group maintained improvement for the 6 months follow up without further treatment, whilst the prucalopride group continued on the drug. This trial is also reviewed on the BMAS Blog.

## Stress urinary incontinence

This one was a surprise! The same research group that published on chronic constipation also performed a large multicentre study on stress incontinence (n=504).[76] Deep needling and EA was used around the lower sacrum and coccyx. The description of depth and angulation seemed safe, and it is possible that the real treatment involved direct pudendal nerve stimulation. Eighteen sessions were performed over 6 weeks, and the sham was non-penetrating. The results compared with sham were comparable with a 12-week programme of pelvic floor exercises. See the BMAS Blog on this trial.

This group went on to test the same EA protocol in mixed urinary incontinence against the established conventional treatment (pelvic floor muscle training plus solifenacin – an antimuscarinic drug) in a large non-inferiority trial (n=467). EA was non-inferior to the conventional treatment. [77] Again see the BMAS blog on the trial.

## Allergic rhinitis

Acupuncture for allergic rhinitis (mixed perennial and seasonal) was evaluated as part of the large trial programme funded by the health insurers in Germany from the late 1990s – the Modellvorhaben Akupunktur. [78,79] A pragmatic trial of acupuncture in addition to usual care compared with usual care alone in 981 patients over a three-month period found that a significant benefit occurred in the acupuncture group, and the ICER was estimated at €17 377 per QALY gained.[75]

Seasonal allergic rhinitis was evaluated subsequently in a large sham controlled trial (n=422).[80] The trial compared 12 sessions over 8 weeks of real acupuncture with a sham that involved gentle needling of points that were not recognised as acupuncture points. A third group had no acupuncture initially but received real acupuncture in the second part of the trial, after 8 weeks. All groups were allowed rescue medication in the form of up to two doses of cetirizine per day, and if their symptoms were not adequately controlled, they could be treated with an oral corticosteroid. The primary outcome was a change in symptoms (Rhinitis Quality of Life Questionnaire [RQLQ]) and need for medication (Rescue Medication Score [RMS]). Secondary outcomes included responder rates, where a responder was defined by a change in RQLQ of at least 0.5 compared with baseline. Real acupuncture was associated with a statistically significant benefit over sham at 7 to 8 weeks (end of treatment), but not at 15 to 16 weeks (approaching the end of the season), when the sham group caught up. Interestingly, the real acupuncture group was still significantly improved in the following year compared with the sham group, regarding both symptoms and medication use. Despite this long-term effect, the economic analysis was restricted to the primary endpoint at 8 and 16 weeks. The ICER for each additional QALY gained by using acupuncture to treat seasonal allergic rhinitis was between €31 241 and €118 889 from a societal perspective, and between €20 807 and €74 585 from a third-party payer's perspective. This does not look likely to be cost effective using contemporary thresholds for cost effectiveness (approximately €50 000 per QALY gain).[81]

The trial was featured in NICE Eyes on Evidence in September 2013,[82] and it was comforting that their editors recognised the clinical significance of the results, a detail that the editors of *Annals of Internal Medicine* felt necessary to caution against.

## Hot flushes

There has been great interest in using acupuncture techniques to reduce vasomotor symptoms associated with the menopause as well as those related to hormone therapy for treatment of breast and prostate cancer.[83–85]

Pragmatic trials have demonstrated clinically relevant effects,[86–89] but sham controlled trials have failed to do so.[90] See the category 'hot flushes' on the BMAS blog for comment on the failure to demonstrate efficacy in RCTs.

Menopausal hot flushes appear to respond to acupuncture to a similar degree as low dose HRT, and better than phytoestrogens.[91] It should be noted that low dose HRT may have similar effects to higher doses when it comes to vasomotor symptoms.[92]

Symptoms related to the use of aromatase inhibitors, including hot flushes and joint pains, appear to respond to acupuncture treatment.[93,94]

Finally, an ingenious NMA has compared the effects of acupuncture in the real treatment groups of RCTs for hot flushes in which either non-penetrating sham devices or shallow needling was used in the control. It seems that the use of non-penetrating sham devices may significantly degrade the effect of real acupuncture.[95] See the BMAS blog for a fuller discussion.

## The huge retrospective observational cohort studies

These studies have been published with increasing frequency since 2017. The majority originate from Taiwan, where almost the entire population is on the same health insurance database. A cohort of 1 million randomly selected patients has been created for research purposes, and this cohort has been analysed for associations between the use of acupuncture and various health outcomes.

There is a similar research database in Korea, and publications from studies on this database started to appear in 2016, but MC did not notice them until 2019.

The following list provides a summary of the associations noted in order of publication date. Please note that this data is observational, and therefore it does not provide proof of cause and effect, but only

associations. Acupuncture is associated with a decreased risk of:

- epilepsy in patients with stroke in Taiwan [96] (aHR 0.74)
- coronary heart disease in patients with fibromyalgia in Taiwan [97] (aHR 0.43)
- coronary heart disease in patients with rheumatoid arthritis in Taiwan [98] (aHR 0.60)
- stroke in patients with depression in Taiwan [99] (aHR 0.49)
- cervical surgery in patients with neck pain in Korea [100] (aHR 0.397)
- knee surgery in patients with knee OA in Korea [101] (aHR 0.273)
- Parkinson's disease in patients with depression in Taiwan [102] (aHR 0.39)
- stroke in patients with fibromyalgia in Taiwan [103] (aHR 0.53)
- major adverse cardiovascular events in patients with hypertension in Korea [104] (aHR 0.83)
- mortality, readmission and reoperation following hip fracture surgery in Taiwan [105] (aHRs 0.41, 0.64, 0.62)
- coronary heart disease in patients with osteoarthritis in Taiwan [106] (aHR 0.33)
- acromioplasty in patients with shoulder pain in Korea [107] (aHR 0.264)
- fracture in patients with OA in Taiwan [108] (aHR 0.57)
- hypertension in patients with chronic spontaneous urticara in Taiwan [109] (aHR 0.57)
- stroke in patients with migraine in Taiwan [110] (aHR 0.4)
- dementia in patients with insomnia in Taiwan [111] (aHR 0.54)
- pressure ulcer in patients with dementia in Taiwan [112]
- depression in patients with primary dysmenorrhoea in Taiwan [113] (64% risk reduction)
- recurrence of Bell's palsy with early use of acupuncture in Korea [114] (aHR 0.8)
- ischaemic stroke in patients with rheumatoid arthritis in Taiwan [115] (aHR 0.57)
- tube placement in patients with dementia in Taiwan [116] (aHR 0.65) – tube refers to urinary catheter, nasogastric tube, or tracheostomy tube
- stroke in patients with insomnia in Taiwan [117] (aHR 0.68)
- dementia in patients with rheumatoid arthritis in Taiwan [118] (aHR 0.55)
- injuries (mainly falls) in patients with stroke in Taiwan [119] (aHR 0.71)

These databases have also been used to assess adverse events related to acupuncture treatment. As a result we can estimate the incidence of pneumothorax following acupuncture in at risk areas of the body (ie thorax, back and neck) as 1.75 per million acupuncture treatments in Taiwan.[120]

The incidence of cellulitis following acupuncture in Taiwan has been estimated as 64.4 per 100 000 courses of treatment (usually a course is 10 treatment sessions in China and the Far East), and the risk is increased in the presence of a variety of comorbid diseases and the presence of varicose veins.[121]

On a more positive note, in a study from Korea, acupuncture was found to be safe in pregnancy, with no increased risk of preterm delivery or stillbirth.[122]

Also from Korea, another study found that acupuncture was not associated with an increased risk of lymphoedema following breast cancer surgery.[123]

Pre-operative acupuncture in patients undergoing lumbar spinal fusion in Korea was not associated with an increased risk of infection; however, the same could not be said for epidural steroid within 2 weeks prior to surgery.[124]

Before leaving the topic of retrospective observational research, there has been one particularly interesting study from the US on the association of the initial healthcare provider for new-onset low back pain with early and long-term opioid use. Seeing a physical therapist or acupuncturist was associated with 10-fold reduction in risk for early use and a 5 to 10-fold reduction in risk for long-term use of opioids. Whilst the number of acupuncturists included was smaller than that of most other providers, the mean odds ratios associated with seeing an acupuncturist were lower than any other group.[125]

## The BMJ Series 2022

In early 2022 a series of open access papers were released in the *BMJ online* and in *BMJ Open* with the series title – Acupuncture: How to improve the evidence base.

They were curated by Dr Yu-Qing 'Madison' Zhang, who completed her PhD in research methods under the wing of the famous Gordon Guyatt.

There are 9 papers in all, although only 8 are published to date.[126–133] They map the evidence from SRs and guidelines, and identify areas of underutilisation as well as area requiring better quality research, and of course there is a discussion of the methodological challenges and guidance for designing high quality acupuncture trials.
See the BMJ Series 2022 category on the BMAS blog, where several topics from this series of papers are discussed.

## Acupuncture in ICU

In a review paper in the journal Nature in 2002,[134] Tracey discussed the anti-inflammatory role of the vagus nerve, focusing on the anti-TNF effect of peripheral acetylcholine release and implied that acupuncture might be a possible method of stimulating this homeostatic response.

In 2014 a team in the US published an experimental trial in a mouse model of sepsis that demonstrated a novel anti-inflammatory mechanism of indirect vagal stimulation.[135] The intervention they used was 15 minutes of EA to the point ST36, and it saved the majority of mice in the experiment from an otherwise fatal outcome. The effect of EA on TNF lasted for 48–72 hours after just 15 minutes of stimulation at ST36.

A further experimental study demonstrated different effects of EA (both reduced mortality and increased lethality) on a murine model of sepsis based on site and intensity of stimulation, and identified the neural pathways involved using sophisticated genomic labelling techniques.[136]

Since vagal stimulators are being used in patients with severe inflammatory arthropathies,[137,138] it is tempting to wonder if self-applied EA to ST36 2 or 3 times a week could have the same effect, and ideally result in a reduction in frequency of inflammatory episodes.

A similar approach has been adopted in patients with sepsis in China, and preliminary reports appear positive, albeit with the usual cautions concerning papers from the region.[139–141]

In October 2021 we saw the first paper for 40 years with acupuncture (specifically EA) in the title published in the journal Nature. This research again used sophisticated genomic labelling in a murine model of sepsis and identified a specific category of nerves present almost exclusively in deep somatic tissues of the limbs, which mediated a low intensity EA effect in recovery from sepsis.[142]

This is a landmark paper because it identifies the substrate for regional tissue specific effects, and therefore can explain why MA or EA at some points will mediate effects that cannot be achieved at other points. This is not point specificity as such, but it is a step towards some form of regional specificity for low intensity EA.

Another landmark occurred in May 2022 when we saw the first evidence of reduced mortality in human patients with sepsis.[143] This SR of adjuvant acupuncture included 17 RCTs with 1099 patients. Nine RCTs with 490 patients provided mortality data at day 28. Pooling of this data in meta-analysis demonstrated a reduction in mortality of 31% from the addition of acupuncture to routine care.

Following on from this in 2023 we had an SR examining the safety of acupuncture in ICU, and it demonstrated a reduction in 28-day mortality of 39%.[144] A further SR demonstrated reduced mechanical ventilation time as well as reduced 28-day mortality of 33%.[145]

## Key to abbreviations

**ARC** – acupuncture in routine care (large cohort studies, some with randomised elements; also part of the German Health Insurance Modellvorhaben; Berlin group)
**ART** – acupuncture randomised trial (part of the German Health Insurance Modellvorhaben – trial phases; Berlin group)
**CGRP** – calcitonin gene-related peptide
**CPM** – conditioned pain modulation
**EA** – electroacupuncture
**GERAC** – German acupuncture trial (part of the German Health Insurance Modellvorhaben; Bochum group)
**GRASP** – German randomized acupuncture trial for chronic shoulder pain
**HR** – hazard ratio (**aHR** – adjusted HR)
**HRQoL** – health-related quality of life
**ICER** – incremental cost effectiveness ratio
**ICU** – intensive care unit
**IDPM** – individual patient data meta-analysis
**MA** – manual acupuncture
**MCID** – minimal clinically important difference
**NMA** – network meta-analysis
**NNT** – number needed to treat
**NSAID** – non-steroidal anti-inflammatory drug
**OA** – osteoarthritis
**PONV** – postoperative nausea and vomiting
**QALY** – quality adjusted life year (parameter used in economic analysis of healthcare interventions)
**RCT** – randomised controlled trial
**SMD** – standardised mean difference
**SR** – systematic review
**TENS** – transcutaneous electrical nerve stimulation
**TNF** – tumour necrosis factor
**TTH** – tension-type headache
**VAS** – visual analogue score (100mm line)
**WOMAC** – Western Ontario and McMaster Universities Osteoarthritis Index

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