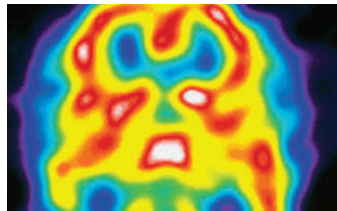


research



Studies of artificial intelligence versus clinicians poor quality
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Trial shows migraine reduced by acupuncture
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Prevalence, incidence, and disability from neck pain globally
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ORIGINAL RESEARCH Systematic review

Artificial intelligence versus clinicians

Nagendran M, Chen Y, Lovejoy CA, et al

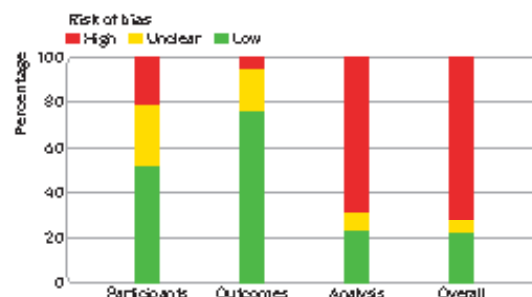
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Study question What are the design, reporting standards, risk of bias, and claims of studies that compared the performance of diagnostic deep learning algorithms for medical imaging with that of expert clinicians?

Methods This systematic review searched Medline, Embase, the Cochrane Central Register of Controlled Trials, and the World Health Organization trial registry for studies comparing the performance of a deep learning algorithm in medical imaging with that of a group of expert clinicians. These studies used medical imaging to predict absolute risk of existing disease or classification into diagnostic groups (eg, disease or non-disease). Adherence to reporting standards was assessed by using CONSORT (consolidated standards of reporting trials) for randomised studies and TRIPOD (transparent reporting of a multivariable prediction model for individual prognosis or diagnosis) for non-randomised studies. Risk of bias was assessed by using the Cochrane risk of bias tool for randomised studies and PROBAST (prediction model risk of bias assessment tool) for non-randomised studies.

Study answer and limitations Only 10 records were found for deep learning randomised clinical trials, two of which have been published (with low risk of bias, except for lack of blinding, and high adherence to reporting standards) and eight are ongoing. Of 81 non-randomised clinical trials identified, only nine were prospective and just six were tested in a real world clinical setting. The median number of experts in the comparator group was only 4 (interquartile range 2-9). Full access to all datasets and code was severely limited (unavailable in 95% and 93% of studies, respectively). The overall risk of bias



PROBAST (prediction model risk of bias assessment tool) risk of bias assessment for non-randomised studies comparing the performance of a deep learning algorithm in medical imaging with a contemporary group of one or more expert clinicians

was high in 58 of 81 studies and adherence to reporting standards was suboptimal (<50% adherence for 12 of 29 TRIPOD items). 61 of 81 studies stated in their abstract that performance of artificial intelligence was at least comparable to (or better than) that of clinicians. Only 31 of 81 studies (38%) stated that further prospective studies or trials were required. A limitation of this review is that the reporting standards are not explicitly designed for studies on deep learning.

What this study adds Few prospective deep learning studies and randomised trials exist in medical imaging. Most non-randomised trials are not prospective, are at high risk of bias, and deviate from existing reporting standards. Data and code availability is lacking in most studies, and human comparator groups are often small. Future studies should diminish risk of bias, enhance real world clinical relevance, improve reporting and transparency, and appropriately temper conclusions.

Funding, competing interests, and data sharing No specific funding or relevant competing interests. Raw data are available on request from the corresponding author. Full details are available on bmj.com.

Study registration PROSPERO CRD42019123605.

Manual acupuncture for migraine

ORIGINAL RESEARCH Multicentre, randomised clinical trial

Manual acupuncture versus sham acupuncture and usual care for prophylaxis of episodic migraine without aura

Xu S, Yu L, Luo X, et al

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Find this at: <http://dx.doi.org/10.1136/bmj.m697>

Study question Is manual acupuncture effective for migraine prophylaxis compared with sham acupuncture and usual care?

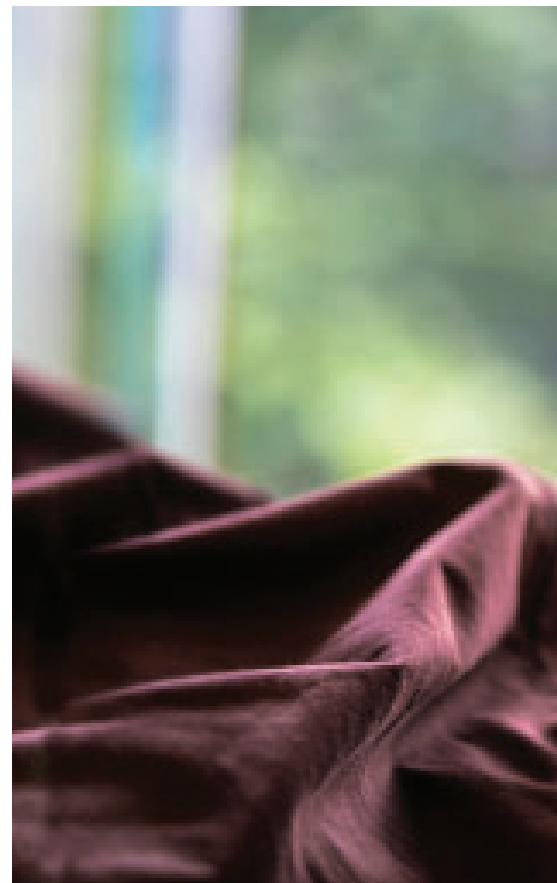
Methods This multicentre, randomised, controlled clinical trial recruited 150 acupuncture naive patients with episodic migraine without aura in seven hospitals in China from 5 June 2016 to 15 November 2018. Participants were randomly allocated to receive 20 sessions of manual acupuncture at true acupuncture points, 20 sessions of non-penetrating sham acupuncture at heterosegmental non-acupuncture points, or usual care over eight weeks. The primary outcomes were change in migraine days and migraine attacks per four weeks during weeks 1 to 20 after randomisation compared with baseline (four weeks before randomisation).

Study answer and limitations Manual acupuncture, compared with sham acupuncture, resulted in significantly greater reductions in the mean number of migraine days (3.9 (SD 3.0) v 2.2 (3.2); adjusted difference -2.1, 95% confidence interval -2.9 to -1.2) and migraine attacks (2.3 (1.7) v 1.6 (2.5); -1.0, -1.5 to -0.5) during weeks 17 to 20 after randomisation. Sham acupuncture resulted in a minor reduction in migraine attacks compared with usual care (1.6 (2.5) v 0.4 (1.3); -0.8, -1.4 to -0.2) during weeks 17 to 20. The major limitation was that the time frame might not be long enough to see a long lasting effect.

What this study adds Manual acupuncture was more effective than sham acupuncture and usual care in reducing migraine headaches.

Funding, competing interests, and data sharing This study was supported by a grant from the National Natural Science Foundation of China (61327902) and a project grant from Hubei University of Chinese Medicine/Hubei Provincial Collaborative Innovation Center of Preventive Treatment by Acupuncture and Moxibustion. The authors declare no competing interests. The raw trial data after de-identification can be shared on request.

Study registration ClinicalTrials.gov NCT02765581.



COMMENTARY New trial moves acupuncture from complementary therapy to evidence based treatment

Migraine is one of the most common and disabling neuropathic pains, affecting at least 10-20% of the population and causing billions of lost days each year. In this issue, Xu and colleagues show that manual acupuncture significantly reduces migraine headaches, compared to both sham acupuncture and usual care.²

One strength of this study is the authors' choice of control intervention. This is a major hurdle for non-pharmacological studies. Only these authors and one previous study of acupuncture have demonstrated successful masking of the sham procedure.³

Xu and colleagues' used a non-penetrating needle for sham acupuncture—essential because

Given that almost 90% of people with frequent migraine have no effective preventive treatment, acupuncture provides a useful additional tool

penetrative sham acupuncture is not inert, and activates pathways involved in pain.⁴ They also used an additional arm of usual treatment (including advice on lifestyle and self-management), controlling for the therapeutic effects of contact with a clinician, which contribute to strong placebo effects in migraine trials.⁶ The study achieved 98% retention and reported no serious adverse events.

The effects of acupuncture are modest (2.1 fewer migraine days per month in the current study), and it is difficult for clinicians to know whether this level of benefit would be noticeable to patients. The authors do not discuss

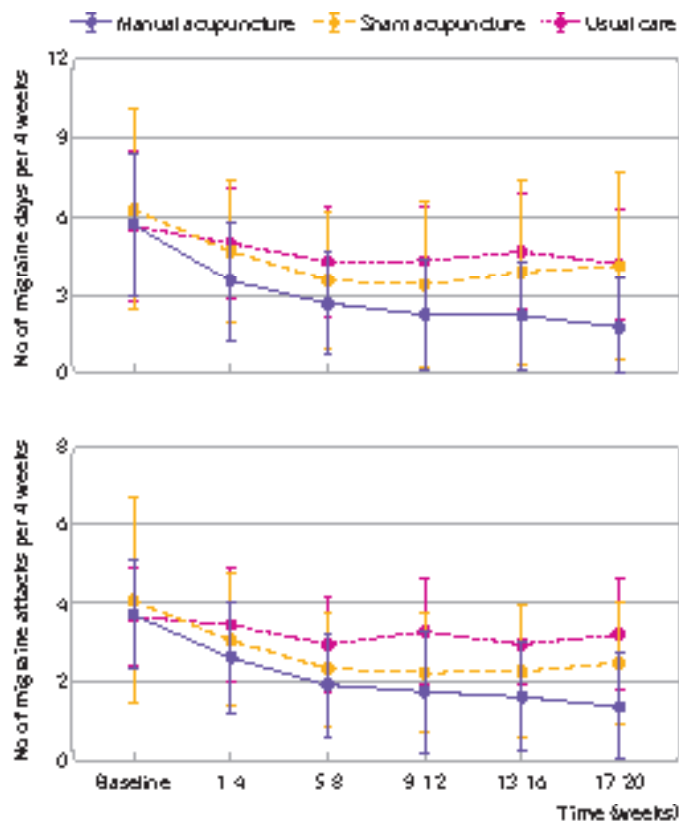
the minimally clinically important difference, and statistical significance does not automatically translate to clinical significance.

The study period was relatively short (20 weeks) and it is not known whether acupuncture resets sensory pathways for a sustained improvement or whether it must be repeated to maintain its effects. Longer term studies are now a priority.

Solid evidence

Xu and colleagues' findings provide a solid evidence base for a non-pharmacological treatment often dismissed as an unproved complementary therapy. Benefits of acupuncture were less than those associated with recently developed preventive treatments (monoclonal antibodies to calcitonin gene related peptide receptors; 3.7 v 2.1 reduction in migraine days per month)⁷ but no head-to-

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Number of migraine days and frequency of migraine attacks per four weeks throughout study period

head comparisons are currently available.

Acupuncture might be a first choice for people who want to avoid pharmacological treatment, or for those who take several drugs with potential interactions. No interactions have been reported between acupuncture and pharmaceutical agents, and acupuncture is associated with no long term adverse events. Pregnancy was an exclusion criterion in Xu and colleagues' study, but adverse events in pregnancy have not been reported in the literature. Acupuncture could be a potential treatment for pregnant women who do not want to take drug treatment.

The mechanism of action through which acupuncture relieves migraine is unclear. The experience of pain is complex, and multiple mechanisms could contribute. One possibility is that acupuncture blocks central processing of pain through alternative stimulation, similar to other

non-pharmacological pain treatments such as transcutaneous electrical nerve stimulation.⁸

Pain sensitive structures in the head and neck connect with cells in the spinal cord, thalamus, and cortex. These same cells also receive input from the limbs, including from established acupuncture points. This convergence might explain acupuncture's effects.⁹ Acupuncture also activates the limbic system, important in emotional responses,² and releases endorphin, a transmitter that potentially reduces pain.¹⁰

The cost effectiveness of manual acupuncture and our ability to upscale its use needs further exploration. The practitioners working in this trial were highly skilled, and had five years' experience. Treatment sessions involved 10 hours of acupuncture in total. This kind of intervention would not be cheap.

Further, a fifth of young adults are needle phobic.¹¹ Other options include electrical or automated systems of acupuncture, although further research and development is required, not least to examine whether automated systems are as effective as acupuncture delivered by human contact.

We now have good evidence that acupuncture is an effective treatment for episodic migraine. Given that almost 90% of people with frequent migraine have no effective preventive treatment, acupuncture provides a useful additional tool in our therapeutic armoury. Xu and colleagues' study helps to move acupuncture from having an unproved status in complementary medicine to an acceptable evidence based treatment.

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Global, regional, and national burden of neck pain in the general population, 1990-2017

Safiri S, Kolahi AA, Hoy D, et al

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Study question What are the point prevalence, annual incidence, and years lived with disability for neck pain, from 1990 to 2017, by age, sex, and sociodemographic index?

Methods A systematic analysis was conducted of data from the Global Burden of Disease Study 2017. New data sources, such as national health surveys and claims data, and new disability weights data, were included. Analyses were stratified by age and sociodemographic index (a composite of sociodemographic factors) and adjusted for comorbidity. Numbers and age standardised

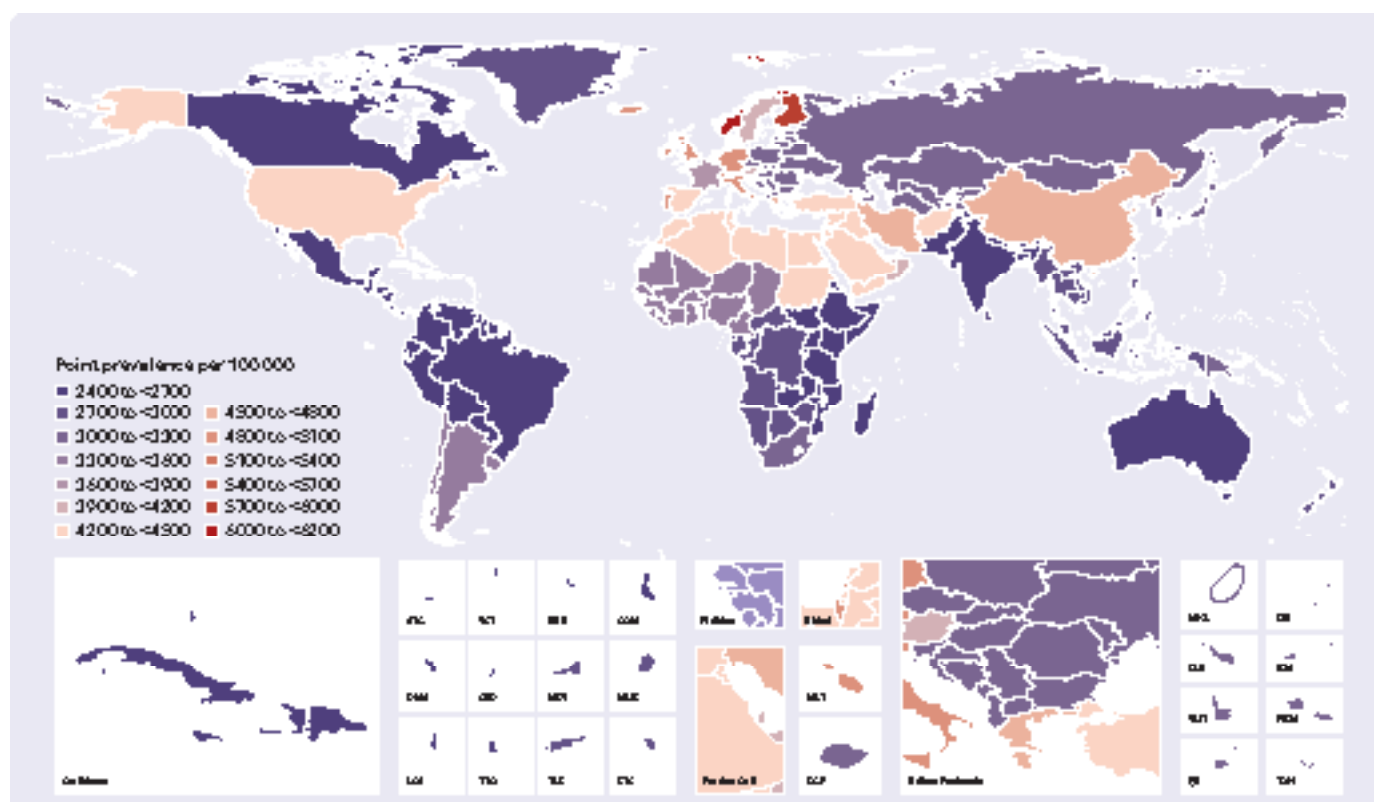
rates of point prevalence, annual incidence, and years lived with disability from neck pain per 100 000 population were compared across regions and countries by age, sex, and sociodemographic index. Estimates were reported with uncertainty intervals.

Study answer and limitations Globally, in 2017 the age standardised point prevalence per 100 000 population for neck pain was 3551.1 (95% uncertainty interval 3139.5 to 3977.9) and the age standardised annual incidence of neck pain per 100 000 was 806.6 (713.7 to 912.5). At the global level too, the number of years lived with disability from neck pain in 2017 was 28.6 million (20.0 to 40.2 million), with an age standardised rate per 100 000 population of 352 (95% uncertainty interval 245.6 to 493.3) years lived with disability. These estimates did not change significantly between 1990 and 2017. Recall bias is possible as data were collected

at five follow-up points over two years. Also, as the severity distributions were derived from the Medical Expenditure Panel Surveys analysis conducted in the USA, these surveys might not be representative of the health state experience for neck pain worldwide.

What this study adds Neck pain is a serious public health issue in the general population, with the highest prevalence in western Europe, East Asia, and North Africa and the Middle East in 2017. Norway, Finland, and Denmark were the countries with the highest age standardised prevalence estimates in 2017.

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Age standardised point prevalence of neck pain per 100 000 population in 2017, by country. ATG=Antigua and Barbuda; VCT=Saint Vincent and the Grenadines; BRB=Barbados; COM=Comoros; DMA=Dominica; GRD=Grenada; MDV=Maldives; MUS=Mauritius; LCA=Saint Lucia; TTO=Trinidad and Tobago; TLS=Timor-Leste; SYC=Seychelles; MLT=Malta; SGP=Singapore; MHL=Marshall Islands; KIR=Kiribati; SLB=Solomon Islands; FSM=Federated States of Micronesia; VUT=Vanuatu; WSM=Samoa; FJI=Fiji; TON=Tonga. Generated from data available at <http://ghdx.healthdata.org/gbd-results-tool>