**Selected by
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Latest Publications You Should Not Miss

**Linde K, Niemann K, Schneider A, Meissner K:
How large are the nonspecific effects of acupuncture?
A meta-analysis of randomized controlled trials.
BMC Medicine 2010;8:75.**

Background: While several recent large randomized trials found clinically relevant effects of acupuncture over no treatment or routine care, blinded trials comparing acupuncture to sham interventions often reported only minor or no differences. This raises the question whether (sham) acupuncture is associated with particularly potent nonspecific effects. We aimed to investigate the size of nonspecific effects associated with acupuncture interventions.

Methods: MEDLINE, Embase, Cochrane Central Register of Controlled Clinical Trials and reference lists were searched up to April 2010 to identify randomized trials of acupuncture for any condition, including both sham and no acupuncture control groups. Data were extracted by one reviewer and verified by a second. Pooled standardized mean differences were calculated using a random effects model with the inverse variance method.

Results: Thirty-seven trials with a total of 5754 patients met the inclusion criteria. The included studies varied strongly regarding patients, interventions, outcome measures, methodological quality and effect sizes reported. Among the 32 trials reporting a continuous outcome measure, the random effects standardized mean difference between sham acupuncture and no acupuncture groups was -0.45 (95% confidence interval, $-0.57, -0.34$; $I^2 = 54\%$; Egger's test for funnel plot asymmetry, $P = 0.25$). Trials with larger effects of sham over no acupuncture reported smaller effects of acupuncture over sham intervention than trials with smaller nonspecific effects ($\beta = -0.39, P = 0.029$).

Conclusions: Sham acupuncture interventions are often associated with moderately large nonspecific effects which could make it difficult to detect small additional specific effects. Compared to inert placebo interventions, effects associated with sham acupuncture might be larger, which would have considerable implications for the design and interpretation of clinical trials.

**Mutter J, Curth A, Naumann J, Deth R; Walach H:
Does inorganic mercury play a role in Alzheimer's
disease? A systematic review and an integrated
molecular mechanism. J Alz Dis 2010;22:357–374**

Mercury is one of the most toxic substances known to humans. It has been introduced into the human environment and has also been widely used in medicine. Since circumstantial evidence exists that the pathology of Alzheimer's disease (AD) might be in part caused or exacerbated by inorganic mercury, we conducted a systematic review using a comprehensive search strategy. Studies were screened according to a predefined protocol. Two reviewers extracted relevant data independent of each other. One thousand and forty one references were scrutinized, and 106 studies fulfilled the inclusion criteria. Most studies were case control or comparative cohort studies. Thirtytwo studies, out of 40 testing memory in individuals exposed to inorganic mercury, found significant memory deficits. Some autopsy studies found increased mercury levels in brain tissues of AD patients. Measurements of mercury levels in blood, urine, hair, nails, and cerebrospinal fluid were inconsistent. *In vitro* models showed that inorganic mercury reproduces all pathological changes seen in AD, and in animal models inorganic mercury produced changes that are similar to those seen in AD. Its high affinity for selenium and selenoproteins suggests that inorganic mercury may promote neurodegenerative disorders via disruption of redox regulation. Inorganic mercury may play a role as a cofactor in the development of AD. It may also increase the pathological influence of other metals. Our mechanistic model describes potential causal pathways. As the single most effective public health primary preventive measure, industrial, and medical usage of mercury should be eliminated as soon as possible.

**Golomb BA, Erickson LC, Koperski S, Sack D, Enkin M,
Howick J: What's in placebos: Who knows?
Analysis of randomized, controlled trials. Ann Intern
Med 2010;153:532–535.**

Background: No regulations govern placebo composition. The composition of placebos can influence trial outcomes and merits reporting.

Purpose: To assess how often investigators specify the composition of placebos in randomized, placebo-controlled trials.

Data Sources: 4 English-language general and internal medicine journals with high impact factors.

Study Selection: 3 reviewers screened titles and abstracts of the journals to identify randomized, placebo-controlled trials published from January 2008 to December 2009.

Data Extraction: Reviewers independently abstracted data from the introduction and methods sections of identified articles, recording treatment type (pill, injection, or other) and whether placebo composition was stated. Discrepancies were resolved by consensus.

Data Synthesis: Most studies did not disclose the composition of the study placebo. Disclosure was less common for pills than for injections and other treatments (8.2% vs. 26.7%; $P = 0.002$).

Limitation: Journals with high impact factors may not be representative.

Conclusion: Placebos were seldom described in randomized, controlled trials of pills or capsules. Because the nature of the placebo can influence trial outcomes, placebo formulation should be disclosed in reports of placebo-controlled trials.

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**National Institute of Complementary Medicine:
Cost effectiveness of complementary medicines.
Australia, August 2010. [www.accesseconomics.com.au/
publicationsreports/getreport.php?report=248&id=317](http://www.accesseconomics.com.au/publicationsreports/getreport.php?report=248&id=317).**

Foreword: In 2009, the National Institute of Complementary Medicine (NICM) commissioned Access Economics to undertake a series of cost effectiveness studies of selected complementary medicine interventions where a reasonable body of evidence for safety and efficacy was available. These were:

- Acupuncture for chronic low back pain;
- St John's wort for mild to moderate depression;
- Omega 3 fish oils for secondary prevention of heart disease;
- Omega 3 fish oils to reduce non steroidal anti-inflammatory drug use in rheumatoid arthritis; and
- A proprietary herbal medicine for pain and inflammation of osteoarthritis.

Details of the analyses undertaken by Access Economics follow. It should be noted that only *direct* health costs are included in these analyses and indirect costs (such as loss of productivity at work) have been excluded. Cost savings would be expected to be higher if indirect costs were included in the analyses.

The findings detailed in this report provide evidence that selected complementary medicine interventions represent cost effective treatment options in an Australian practice context for specific medical conditions. Further, interventions were cost effective despite the addition of the GST to complementary medicine products.

In summary: Acupuncture for chronic low back pain was found to be cost effective if used as a *complement* to standard care (medication, physiotherapy, exercises, education), although not generally cost effective when used as a *replacement* to standard care (unless co-morbidity of depression is included).

Based on analyses of recent clinical trials St John's wort was determined to be cost effective compared to standard antidepressants for patients with mild to moderate (not severe) depression. The main driver for cost effectiveness is the lower unit cost of St. John's wort.

Fish oils rich in omega 3 fatty acids are highly cost effective when used as an adjunctive treatment in people with a history of coronary heart disease, achieving reduced death and morbidity. These findings are consistent

with other international studies. Fish oils, however, were not cost effective in reducing non steroidal anti-inflammatory drug use in rheumatoid arthritis.

Phytodolor, a proprietary herbal medicine, was found to be cost saving in managing osteoarthritis compared with the principal non steroidal anti-inflammatory drug Diclofenac.

This report is an important component of advancing our knowledge and understanding of Complementary medicine, and supporting informed choices for individual care.

**Jäger T, Scherr C, Simon M, Heusser P, Baumgartner S:
Effects of homeopathic Arsenicum album, nosode,
and gibberellic acid preparations on the growth rate
of arsenic-impaired duckweed (*Lemna gibba* L.).
Scientific World J 2010;10:2112-2129.**

This study evaluated the effects of homeopathically potentized Arsenicum album, nosode, and gibberellic acid in a bioassay with arsenic-stressed duckweed (*Lemna gibba* L.). The test substances were applied in nine potency levels (17 ×, 18 ×, 21 ×–24 ×, 28 ×, 30 ×, 33 ×) and compared with controls (unsuccussed and succussed water) regarding their influence on the plants' growth rate. Duckweed was stressed with arsenic(V) for 48 h. Afterwards, plants grew in either potentized substances or water controls for 6 days. Growth rates of frond (leaf) area and frond number were determined with a computerized image analysis system for different time intervals (days 0–2, 2–6, 0–6). Five independent experiments were evaluated for each test substance. Additionally, five water control experiments were analyzed to investigate the stability of the experimental setup (systematic negative control experiments). All experiments were randomized and blinded. The test system exhibited a low coefficient of variation ($\approx 1\%$). Unsuccussed and succussed water did not result in any significant differences in duckweed growth rate. Data from the control and treatment groups were pooled to increase statistical power. Growth rates for days 0–2 were not influenced by any homeopathic preparation. Growth rates for days 2–6 increased after application of potentized Arsenicum album regarding both frond area ($p < 0.001$) and frond number ($p < 0.001$), and by application of potentized nosode (frond area growth rate only, $p < 0.01$). Potencies of gibberellic acid did not influence duckweed growth rate. The systematic negative control experiments did not yield any significant effects. Thus, false-positive results can be excluded with high certainty. To conclude, the test system with *L. gibba* impaired by arsenic(V) was stable and reliable. It yielded evidence for specific effects of homeopathic Arsenicum album preparations and it will provide a valuable tool for future experiments that aim at revealing the mode of action of homeopathic preparations. It may also be useful to investigate the influence of external factors (e.g., heat, electromagnetic radiation) on the effects of homeopathic preparations.

Kienle GS, Kiene H: Review article: Influence of Viscum album L (European mistletoe) extracts on quality of life in cancer patients: A systematic review of controlled clinical studies. Integr Cancer Ther 2010;9:142

Objective: To evaluate controlled clinical studies on the efficacy and effectiveness of *Viscum album* for quality of life (QoL) in cancer.

Materials and methods: The authors conducted a search of 7 electronic databases and reference lists and had extensive consultations with experts. They carried out a criteria-based assessment of methodological study quality.

Results: The authors identified 26 randomized controlled trials (RCTs) and 10 non-RCTs that investigated the influence of *V. album* extracts (VAEs) on QoL in malignant diseases; 26 studies assessed patient-reported QoL. Questionnaires were mostly well-established and validated. Half of the studies investigated VAEs concomitant with chemotherapy, radiotherapy, or surgery.

Some studies were well-designed, whereas others had minor or major methodological weaknesses. Among the 26 RCTs, 22 reported a QoL benefit, 3 indicated no difference, and 1 did not report any result. All the non-RCTs reported a QoL benefit. Of the studies with higher methodological quality, most reported a benefit, whereas 1 found no difference. Improvements were mainly in regard to coping, fatigue, sleep, exhaustion, energy, nausea, vomiting, appetite, depression, anxiety, ability to work, and emotional and functional well-being in general and, less consistently, in regard to pain, diarrhea, general performance, and side-effects of conventional treatments. VAEs were well tolerated.

Conclusions: VAEs seem to have an impact on QoL and reduction of side effects of conventional therapies (chemotherapy, radiation) in experimental trials as well as in routine daily application. The influence on fatigue especially should be investigated further.

Hunt P, Khosla R: Are drug companies living up to their human rights responsibilities? The perspective of the former United Nations Special Rapporteur (2002–2008). PLoS Med 2010;7:9.

Background to the debate: The human rights responsibilities of drug companies have been considered for years by nongovernmental organizations, but were most sharply defined in a report by the UN Special Rapporteur on the right to health, submitted to the United Nations General Assembly in August 2008. The 'Human Rights Guidelines for Pharmaceutical Companies in relation to Access to Medicines' include responsibilities for transparency, management, monitoring and accountability, pricing, and ethical marketing, and against lobbying for more protection in intellectual property laws, applying for patents for trivial modifications of existing medicines, inappropriate drug promotion, and excessive pricing. Two years after the release of the Guidelines, the PLoS Medicine Debate asks whether drug companies are living up to their human rights responsibilities.

Sofia Gruskin and Zyde Raad from the Harvard School of Public Health say more assessment is needed of such responsibilities; GERALYN Ritter, Vice President of Global Public Policy and Corporate Responsibility at Merck & Co., argues that multiple stakeholders could do more to help States deliver the right to health; and Paul Hunt and Rajat Khosla introduce Mr. Hunt's work as the UN Special Rapporteur on the right to the highest attainable standard of health, regarding the human rights responsibilities of pharmaceutical companies and access to medicines.

Werner C, Sobiraj A, Sundrum A: Efficacy of homeopathic and antibiotic treatment strategies in cases of mild and moderate bovine clinical mastitis. J Dairy Research 2010;77:460–467.

The objective of this clinical control trial was to examine the effectiveness of the classical homeopathic treatment strategy in cases of mild and moderate bovine clinical mastitis in comparison with antibiotic and placebo treatments. Owing to characteristics of the selected herds, only cases of clinical mastitis caused by environmental pathogens and clinical cases with negative bacteriological result in the pre-treatment milk sample were included in the trial. A total of 136 lactating dairy cows with 147 affected quarters from four herds in Germany were randomly allocated to three treatment groups. The cows were examined on days 0, 1, 2 and on days 7, 14, 28 and 56 post initial infection to assess clinical signs. Simultaneously, with the exception of days 1 and 2, quarter milk samples for laboratory examinations (bacteriology, somatic cell count) were collected to assess bacteriological and cytological cure rates. On days 28 and 56, treatment strategies did not differ significantly with respect to the clinical outcomes and the total cure rate in cases of bacteriological negative mastitis ($n = 56$). In cases of pathogen positive mastitis ($n = 91$), the cure rate after 4 and 8 weeks was similar between the two treatment strategies, homeopathy and antibiotic treatment, but the difference between the homeopathic and the placebo treatment at day 56 was significant ($P < 0.05$). The results indicate a therapeutic effect of homeopathic treatment in cases of mild and moderate clinical mastitis. However, independent of treatment strategy and bacteriological status, the total cure rate was on a low level, revealing limitations in the effectiveness of both antibiotic and homeopathic treatment strategies.