**Selected by
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Latest Publications You Should Not Miss

Teut M, Dahler J, Hirschberg U, Lüdtke R, Albrecht H, Witt CM: Homeopathic drug proving of *Okoubaka aubrevillei*: a randomised placebo-controlled trial. *Trials* 2013;14:96.

Background: Homeopathic drug proving is a basic concept in homeopathy. This study aimed to record symptoms produced by a homeopathic drug compared with placebo.

Methods: This multicentre, randomised, double-blind, placebo-controlled phase 1 trial consisted of a 7-day run-in period, a 5-day intervention period and a 16-day post-intervention observation period. Subjects, investigators and statisticians were blinded for intervention groups and identity of the homeopathic drug. Subjects in the intervention group received *Okoubaka aubrevillei* (potency C12) and subjects in the placebo group received the optically identical sucrose globules. Dosage in both groups was five globules taken five times per day over a maximum period of 5 days. Subjects documented the symptoms they experienced in a semi-structured online diary. The primary outcome parameter was the number of characteristic proving symptoms compared with placebo after a period of 3 weeks. Characteristic symptoms were categorised using content analysis. Secondary outcome parameters were the qualitative differences in profiles of characteristic and proving symptoms and the total number of all proving symptoms. The number of symptoms was quantitatively analysed on an intention-to-treat basis using analyses of covariance with the subject's expectation and baseline values as covariates.

Results: Thirty-one subjects were included (19 *Okoubaka* and 12 placebo). Data for 29 participants could be analysed. No significant differences in number of characteristic symptoms in both groups were observed between *Okoubaka* (mean $\pm$ standard deviation 5.4 ± 6.0) and placebo (4.9 ± 5.6). The odds ratio for observation of a characteristic symptom was 1.11 (95% confidence interval 0.4 to 3.05, $P = 0.843$). Females and subjects expecting a higher number of symptoms at baseline or feeling more sensitive to homeopathic drugs experienced more characteristic

symptoms regardless of allocation. The qualitative analysis showed an inter-coder reliability of 0.69 (95% confidence interval 0.62 to 0.76). The qualitative comparison of symptom profiles was inconclusive.

Conclusions: Combined results of qualitative and quantitative methods did not result in a significant difference of characteristic proving symptoms between *O. aubrevillei* C12 and placebo. The qualitative comparison of the symptom profiles leaves some open questions. The nocebo effect might be a plausible explanation for most of the phenomena observed in this trial.

Tefikow S, Barth J, Maichrowitz S, Beelmann A, Strauss B, Rosendahl J: Efficacy of hypnosis in adults undergoing surgery or medical procedures: a meta-analysis of randomized controlled trials. *Clin Psychol Rev* 2013;33:623–636.

This meta-analysis investigates the efficacy of hypnosis in adults undergoing surgical or medical procedures compared to standard care alone or an attention control. Through a comprehensive literature search $N = 34$ eligible randomized controlled trials (RCTs) were included, comprising a total of 2,597 patients. Random effects meta-analyses revealed positive treatment effects on emotional distress ($g = 0.53$, CI 95% (0.37; 0.69)), pain ($g = 0.44$, CI 95% (0.26; 0.61)), medication consumption ($g = 0.38$, CI 95% (0.20; 0.56)), physiological parameters ($g = 0.10$, CI 95% (0.02; 0.18)), recovery ($g = 0.25$, CI 95% (0.04; 0.46)), and surgical procedure time ($g = 0.25$, CI 95% (0.12; 0.38)). In conclusion, benefits of hypnosis on various surgically relevant outcomes were demonstrated. However, the internal validity of RCTs seems limited and further high methodological quality RCTs are needed to strengthen the promising evidence of hypnosis for adults undergoing surgery or medical procedures.

Underwood M, Lamb SE, Eldridge S, Sheehan B, Slowther AM, Spencer A, Thorogood M, Atherton N, Bremner SA, Devine A, Diaz-Ordaz K, Ellard DR, Potter R, Spanjers K, Taylor SJ: Exercise for depression in elderly residents of care homes: a cluster-randomised controlled trial. Lancet 2013; 382:41–49.

Background: Depression is common and is associated with poor outcomes among elderly care-home residents. Exercise is a promising low-risk intervention for depression in this population. We tested the hypothesis that a moderate intensity exercise programme would reduce the burden of depressive symptoms in residents of care homes.

Methods: We did a cluster-randomised controlled trial in care homes in two regions in England; northeast London, and Coventry and Warwickshire. Residents aged 65 years or older were eligible for inclusion. A statistician independent of the study randomised each home (1 to 1.5 ratio, stratified by location, minimised by type of home provider (local authority, voluntary, private and care home, private and nursing home) and size of home (<32 or ≥32 residents)) into intervention and control groups. The intervention package included depression awareness training for care-home staff, 45 min physiotherapist-led group exercise sessions for residents (delivered twice weekly), and a whole home component designed to encourage more physical activity in daily life. The control consisted of only the depression awareness training. Researchers collecting follow-up data from individual participants and the participants themselves were inevitably aware of home randomisation because of the physiotherapists' activities within the home. A researcher masked to study allocation coded NHS routine data. The primary outcome was number of depressive symptoms on the geriatric depression scale-15 (GDS-15). Follow-up was for 12 months. This trial is registered with ISRCTN Register, number ISRCTN43769277.

Findings: Care homes were randomised between Dec 15, 2008, and April 9, 2010. At randomisation, 891 individuals in 78 care homes (35 intervention, 43 control) had provided baseline data. We delivered 3,191 group exercise sessions attended on average by five study participants and five non-study residents. Of residents with a GDS-15 score, 374 of 765 (49%) were depressed at baseline; 484 of 765 (63%) provided 12 month follow-up scores. Overall the GDS-15 score was 0.13 (95% CI –0.33 to 0.60) points higher (worse) at 12 months for the intervention group compared with the control group. Among residents depressed at baseline, GDS-15 score was 0.22 (95% CI –0.52 to 0.95) points higher at 6 months in the intervention group than in the control group. In an end of study cross-sectional analysis, including 132 additional residents joining after randomisation, the odds of being depressed were 0.76 (95% CI 0.53 to 1.09) for the intervention group compared with the control group.

Interpretation: This moderately intense exercise programme did not reduce depressive symptoms in residents of care homes. In this frail population, alternative strategies to manage psychological symptoms are required.

Bernardy K, Klose P, Busch AJ, Choy EHS, Häuser W: Cognitive behavioural therapies for fibromyalgia. Cochrane Database Syst Rev 2013;10:CD009796.

Background: Fibromyalgia (FM) is a clinically well-defined chronic condition of unknown aetiology characterized by chronic widespread pain that often co-exists with sleep disturbances, cognitive dysfunction and fatigue. Patients often report high disability levels and negative mood. Psy-

chotherapies focus on reducing key symptoms, improving daily functioning, mood and sense of personal control over pain.

Objectives: To assess the benefits and harms of cognitive behavioural therapies (CBTs) for treating FM at end of treatment and at long-term (at least six months) follow-up.

Search methods: We searched the Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library 2013, Issue 8), MEDLINE (1966 to 28 August 2013), PsycINFO (1966 to 28 August 2013) and SCOPUS (1980 to 28 August 2013). We searched <http://www.clinicaltrials.gov> (web site of the US National Institutes of Health) and the World Health Organization Clinical Trials Registry Platform (ICTRP) (<http://www.who.int/ictpr/en/>) for ongoing trials (last search 28 August, 2013), and the reference lists of reviewed articles.

Selection criteria: We selected randomised controlled trials of CBTs with children, adolescents and adults diagnosed with FM.

Data collection and analysis: The data of all included studies were extracted and the risks of bias of the studies were assessed independently by two review authors. Discrepancies were resolved by discussion.

Main results: Twenty-three studies with 24 study arms with CBTs were included. A total of 2,031 patients were included; 1,073 patients in CBT groups and 958 patients in control groups. Only two studies were without any risk of bias. The GRADE quality of evidence of the studies was low. CBTs were superior to controls in reducing pain at end of treatment by 0.5 points on a scale of 0 to 10 (standardised mean difference (SMD) –0.29; 95% confidence interval (CI) –0.49 to –0.17) and by 0.6 points at long-term follow-up (median 6 months) (SMD –0.40; 95% CI –0.62 to –0.17); in reducing negative mood at end of treatment by 0.7 points on a scale of 0 to 10 (SMD –0.33; 95% CI –0.49 to –0.17) and by 1.3 points at long-term follow-up (median 6 months) (SMD –0.43; 95% CI –0.75 to –0.11); and in reducing disability at end of treatment by 0.7 points on a scale of 0 to 10 (SMD –0.30; 95% CI –0.51 to –0.08) and at long-term follow-up (median 6 months) by 1.2 points (SMD –0.52; 95% CI –0.86 to –0.18). There was no statistically significant difference in dropout rates for any reasons between CBTs and controls (risk ratio (RR) 0.94; 95% CI 0.65 to 1.35).

Author's conclusions: CBTs provided a small incremental benefit over control interventions in reducing pain, negative mood and disability at the end of treatment and at long-term follow-up. The dropout rates due to any reason did not differ between CBTs and controls.

MacPherson H, Richmond S, Bland M, Brealey S, Gabe R, Hopton A, Keding A, Lansdown H, Perren S, Sculpher M, Spackman E, Torgerson D, Watt I: Acupuncture and counselling for depression in primary care: a randomised controlled trial. PLoS Med 2013;10:e1001518.

Background: Depression is a significant cause of morbidity. Many patients have communicated an interest in nonpharmacological therapies to their general practitioners. Systematic reviews of acupuncture and counselling for depression in primary care have identified limited evidence. The aim of this study was to evaluate acupuncture versus usual care and counselling versus usual care for patients who continue to experience depression in primary care.

Methods and findings: In a randomised controlled trial, 755 patients with depression (Beck Depression Inventory BDI-II score ≥20) were recruited from 27 primary care practices in the North of England. Patients were randomised to one of three arms using a ratio of 2:2:1 to acupuncture (302), counselling (302), and usual care alone (151). The primary outcome was the difference in mean Patient Health Questionnaire (PHQ-9) scores at 3 months with secondary analyses over 12 months follow-up. Analysis was by intention-to-treat. PHQ-9 data were available for 614 pa-

tients at 3 months and 572 patients at 12 months. Patients attended a mean of ten sessions for acupuncture and nine sessions for counselling. Compared to usual care, there was a statistically significant reduction in mean PHQ-9 depression scores at 3 months for acupuncture (22.46, 95% CI 23.72 to 21.21) and counselling (21.73, 95% CI 23.00 to 20.45), and over 12 months for acupuncture (21.55, 95% CI 22.41 to 20.70) and counselling (21.50, 95% CI 22.43 to 20.58). Differences between acupuncture and counselling were not significant. In terms of limitations, the trial was not designed to separate out specific from non-specific effects. No serious treatment-related adverse events were reported.

Conclusions: In this randomised controlled trial of acupuncture and counselling for patients presenting with depression, after having consulted their general practitioner in primary care, both interventions were associated with significantly reduced depression at 3 months when compared to usual care alone.

Mayo-Wilson E, Montgomery P: Media-delivered cognitive behavioural therapy and behavioural therapy (self-help) for anxiety disorders in adults. Cochrane Database Syst Rev 2013;9:CD005330.

Background: Anxiety disorders are the most common mental health problems. They are chronic and unremitting. Effective treatments are available, but access to services is limited. Media-delivered behavioural and cognitive behavioural interventions (self-help) aim to deliver treatment with less input from professionals compared with traditional therapies.

Objectives: To assess the effects of media-delivered behavioural and cognitive behavioural therapies for anxiety disorders in adults.

Search methods: Published and unpublished studies were considered without restriction by language or date. The Cochrane Depression, Anxiety and Neurosis Review Group's Specialized Register (CCDANCTR) was searched all years to 1 January 2013. The CCDANCTR includes relevant randomised controlled trials from the following bibliographic databases: The Cochrane Library (all years), EMBASE (1974 to date), MEDLINE (1950 to date) and PsycINFO (1967 to date). Complementary searches were carried out on Ovid MEDLINE (1950 to 23 February 2013) and PsycINFO (1987 to February, Week 2, 2013), together with International trial registries (the trials portal of the World Health Organization (ICTRP) and ClinicalTrials.gov). Reference lists from previous meta-analyses and reports of randomised controlled trials were checked, and authors were contacted for unpublished data.

Selection criteria: Randomised controlled trials of media-delivered behavioural or cognitive behavioural therapy in adults with anxiety disorders (other than post-traumatic stress disorder) compared with no intervention (including attention/relaxation controls) or compared with face-to-face therapy.

Data collection and analysis: Both review authors independently screened titles and abstracts. Study characteristics and outcomes were extracted in duplicate. Outcomes were combined using random-effects models, and tests for heterogeneity and for small study bias were conducted. We examined subgroup differences by type of disorder, type of intervention provided, type of media, and recruitment methods used.

Main results: One hundred and one studies with 8,403 participants were included; 92 studies were included in the quantitative synthesis. These trials compared several types of media-delivered interventions (with varying levels of support) with no treatment and with face-to-face interventions. Inconsistency and risk of bias reduced our confidence in the overall results. For the primary outcome of symptoms of anxiety, moderate-quality evidence showed medium effects compared with no intervention (standardised mean difference (SMD) 0.67, 95% confidence interval (CI) 0.55 to 0.80; 72 studies, 4,537 participants), and low-quality

evidence of small effects favoured face-to-face therapy (SMD -0.23, 95% CI -0.36 to -0.09; 24 studies, 1,360 participants). The intervention was associated with greater response than was seen with no treatment (risk ratio (RR) 2.34, 95% CI 1.81 to 3.03; 21 studies, 1,547 participants) and was not significantly inferior to face-to-face therapy in these studies (RR 0.78, 95% CI 0.56 to 1.09; 10 studies, 575 participants), but the latter comparison included versions of therapies that were not as comprehensive as those provided in routine clinical practice. Evidence suggested benefit for secondary outcome measures (depression, mental-health related disability, quality of life and dropout), but this evidence was of low to moderate quality. Evidence regarding harm was lacking.

Conclusion: Self-help may be useful for people who are not able or are not willing to use other services for people with anxiety disorders; for people who can access it, face-to-face cognitive behavioural therapy is probably clinically superior. Economic analyses were beyond the scope of this review. Important heterogeneity was noted across trials. Recent interventions for specific problems that incorporate clinician support may be more effective than transdiagnostic interventions (i.e. interventions for multiple disorders) provided with no guidance, but these issues are confounded in the available trials. Although many small trials have been conducted, the generalisability of their findings is limited. Most interventions tested are not available to consumers. Self-help has been recommended as the first step in the treatment of some anxiety disorders, but the short-term and long-term effectiveness of media-delivered interventions has not been established. Large, pragmatic trials are needed to evaluate and to maximise the benefits of self-help interventions.

Liu ZL, Xie LZ, Zhu J, Li GQ, Grant SJ, Liu JP: Herbal medicines for fatty liver diseases. Cochrane Database Syst Rev 2013;24:CD009059.

Background: Fatty liver disease is potentially a reversible condition that may lead to end-stage liver disease. Since herbal medicines such as *Crataegus pinnatifida* and *Salvia miltiorrhiza* have increasingly been used in the management of fatty liver disease, a systematic review on herbal medicine for fatty liver disease is needed.

Objectives: To assess the beneficial and harmful effects of herbal medicines for people with alcoholic or non-alcoholic fatty liver disease.

Search methods: We searched The Cochrane Hepato-Biliary Group Controlled Trials Register, the Cochrane Central Register of Controlled Trials (CENTRAL) (Issue 3, 2012), MEDLINE, EMBASE, and Science Citation Index Expanded to 1 March 2012. We also searched the Chinese BioMedical Database, Traditional Chinese Medical Literature Analysis and Retrieval System, China National Knowledge Infrastructure, Chinese VIP Information, Chinese Academic Conference Papers Database and Chinese Dissertation Database, and the Allied and Complementary Medicine Database to 2 March 2012.

Selection criteria: We included randomised clinical trials comparing herbal medicines with placebo, no treatment, a pharmacological intervention, or a non-pharmacological intervention such as diet or lifestyle, or Western interventions in participants with fatty liver disease.

Data collection and analysis: Two review authors extracted data independently. We used the 'risk of bias' tool to assess the risk of bias of the included trials. We assessed the following domains: random sequence generation, allocation concealment, blinding, incomplete outcome data, selective outcome reporting, and other sources of bias. We presented the effects estimates as risk ratios (RR) with 95% confidence intervals (CI) or as mean differences (MD) with 95% CI, depending on the variables of the outcome measures.

Main results: We included 77 randomised clinical trials, which included 6,753 participants with fatty liver disease. The risks of bias (overestimation of benefits and underestimation of harms) was high in all tri-

als. The mean sample size was 88 participants (ranging from 40 to 200 participants) per trial. Seventy-five different herbal medicine products were tested. Herbal medicines tested in the randomised trials included single-herb products (*Gynostemma pentaphyllum*, *Panax notoginseng*, and *Prunus armeniaca*), proprietary herbal medicines commercially available, and combination formulas prescribed by practitioners. The most commonly used herbs were *Crataegus pinnatifida*, *Salvia miltiorrhiza*, *Alisma orientalis*, *Bupleurum chinense*, *Cassia obtusifolia*, *Astragalus membranaceus*, and *Rheum palmatum*. None of the trials reported death, hepatic-related morbidity, quality of life, or costs. A large number of trials reported positive effects on putative surrogate outcomes such as serum aspartate aminotransferase, alanine aminotransferase, glutamyltransferase, alkaline phosphatases, ultrasound, and computed tomography scan. Twenty-seven trials reported adverse effects and found no significant difference between herbal medicines versus control. However, the risk of bias of the included trials was high. The outcomes were ultrasound

findings in 22 trials, liver computed tomography findings in eight trials, aspartate aminotransferase levels in 64 trials, alanine aminotransferase activity in 77 trials, and glutamyltransferase activities in 44 trials. Six herbal medicines showed statistically significant beneficial effects on ultrasound, four on liver computed tomography, 42 on aspartate aminotransferase activity, 49 on alanine aminotransferase activity, three on alkaline phosphatases activity, and 32 on glutamyltransferase activity compared with control interventions.

Conclusions: Some herbal medicines seemed to have positive effects on aspartate aminotransferase, alanine aminotransferase, ultrasound, and computed tomography. We found no significant difference on adverse effects between herbal medicine and control groups. The findings are not conclusive due to the high risk of bias of the included trials and the limited number of trials testing individual herbal medicines. Accordingly, there is also high risk of random errors.