**Selected by
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Latest Publications You Should Not Miss

Bell IR, Howerter A, Jackson N, Aickin M, Baldwin CM, Bootzin RR: Effects of homeopathic medicines on polysomnographic sleep of young adults with histories of coffee-related insomnia. *Sleep Med* 2011; 12:505–511.

Background: Homeopathy, a common form of alternative medicine worldwide, relies on subjective patient reports for diagnosis and treatment. Polysomnography offers a modern methodology for evaluating the objective effects of taking homeopathic remedies that clinicians claim exert effects on sleep quality in susceptible individuals. Animal studies have previously shown changes in non rapid eye movement sleep with certain homeopathic remedies.

Methods: Young adults of both sexes (ages 18–31) with above-average scores on standardized personality scales for either cynical hostility or anxiety sensitivity (but not both) and a history of coffee-induced insomnia participated in the month-long study. At-home polysomnographic recordings were obtained on successive pairs of nights once per week for a total of eight recordings (nights 1, 2, 8, 9, 15, 16, 22, 23). Subjects (N = 54) received placebo pellets on night 8 (single-blind) and verum pellets on night 22 (double-blind) in 30c doses of one of two homeopathic remedies, Nux Vomica or Coffea Cruda. Subjects completed daily morning sleep diaries and weekly Pittsburgh sleep quality index scales, as well as profile of mood states scales at bedtime on polysomnography nights.

Results: Verum remedies significantly increased PSG total sleep time and NREM, as well as awakenings and stage changes. Changes in actigraphic and self-rated scale effects were not significant.

Conclusions: The study demonstrated the feasibility of using in-home, all-night sleep recordings to study homeopathic remedy effects. Findings are similar though not identical to those reported in animals with the same remedies. Possible mechanisms include initial disruption of the non-linear dynamics of sleep patterns by the verum remedies.

Ahmed I, Sutton AJ, Riley RD: Assessment of publication bias, selection bias, and unavailable data in meta-analyses using individual participant data: a database survey. *BMJ* 2012;344:d7762.

Objective: To examine the potential for publication bias, data availability bias, and reviewer selection bias in recently published meta-analyses that use individual participant data and to investigate whether authors of such meta-analyses seemed aware of these issues.

Design: In a database of 383 meta-analyses of individual participant data that were published between 1991 and March 2009, we surveyed the 31 most recent meta-analyses of randomised trials that examined whether an intervention was effective. Identification of relevant articles and data extraction was undertaken by one author and checked by another.

Results: Only nine (29%) of the 31 meta-analyses included individual participant data from 'grey literature' (such as unpublished studies) in their primary meta-analysis, and the potential for publication bias was discussed or investigated in just 10 (32%). Sixteen (52%) of the 31 meta-analyses did not obtain all the individual participant data requested, yet five of these (31%) did not mention this as a potential limitation, and only six (38%) examined how trials without individual participant data might affect the conclusions. In nine (29%) of the meta-analyses reviewer selection bias was a potential issue, as the identification of relevant trials was either not stated or based on a more selective, non-systematic approach. Investigation of four meta-analyses containing data from ≥ 10 trials revealed one with an asymmetric funnel plot consistent with publication bias, and the inclusion of studies without individual participant data revealed additional heterogeneity between trials.

Conclusions: Publication, availability, and selection biases are a potential concern for meta-analyses of individual participant data, but many reviewers neglect to examine or discuss them. These issues warn against uncritically viewing any meta-analysis that uses individual participant data as the most reliable. Reviewers should seek individual participant data from all studies identified by a systematic review; include, where possible, aggregate data from any studies lacking individual participant data to consider their potential impact; and investigate funnel plot asymmetry in line with recent guidelines.

Flatt J: Decontextualized versus lived worlds: critical thoughts on the intersection of evidence, lifeworld, and values. J Altern Complement Med 2012;18:513–521.

Background: Numerous studies and trials are conducted under the evidence-based complementary and alternative medicine (EBCAM) paradigm. Some individuals view the results generated by this approach as symbolic evidential proof of complementary medicine, and as representative of practice. Such evaluations are made even though the ability to capture and reflect clinical reality by the methods used is questioned. The effect of this type of research on complementary medicine researchers and practitioners has received minimal consideration, and this article explores this subject by critically reviewing the literature and theorizing the effects on the lifeworld and values of those embodied by EBCAM.

Methods: This review accesses the discourse of various disciplines involved with, and commenting on, complementary medicine research. Collected literature is collated within specified limits, subjected to argumentation analysis, and synthesized within a critical theory methodology. Emergent themes are examined, and the effects of EBCAM on holistic researcher and practitioner lifeworld and values are theorized via the colonization framework of critical social theorist Jürgen Habermas.

Results: The use of an evidence-based medicine research model to investigate complementary medicine practice is not well regarded by those who critically examine its use. Within a critical theory framework, the generation and application of research resulting from EBCAM is viewed as a philosophically incongruent process arising from a dominative discourse that can colonize lifeworld. This can result in a variety of pathological symptoms that may have a detrimental effect.

Conclusions: The application of EBCAM has the theoretical potential to damage complementary medicine culture, profession, and practice. Its ongoing use requires thought, attention, and careful revision, taking into account the lifeworld and values of researchers and practitioners. If this inclusive view can occur, knowledge generation with relevance to the whole of the professions could proceed.

Hróbjartsson A, Kaptchuk TJ, Miller FG: Placebo effect studies are susceptible to response bias and to other types of biases. J Clin Epidemiol 2011;64:1223–1229.

Objective: Investigations of the effect of placebo are often challenging to conduct and interpret. The history of placebo shows that assessment of its clinical significance has a real potential to be biased. We analyze and discuss typical types of bias in studies on placebo.

Study Design and Setting: A methodological analysis and discussion.

Results: The inherent nonblinded comparison between placebo and no-treatment is the best research design we have in estimating effects of placebo, both in a clinical and in an experimental setting, but the difference between placebo and no-treatment remains an approximate and fairly crude reflection of the true effect of placebo interventions. A main problem is response bias in trials with outcomes that are based on patients' reports. Other biases involve differential co-intervention and patient dropouts, publication bias, and outcome reporting bias. Furthermore, extrapolation of results to a clinical settings are challenging because of a lack of clear identification of the causal factors in many clinical trials, and the nonclinical setting and short duration of most laboratory experiments.

Conclusions: Creative experimental efforts are needed to assess rigorously the clinical significance of placebo interventions and investigate the component elements that may contribute to the therapeutic benefit.

Kwak SM, Myung S-K, Lee YJ, Seo HG; for the Korean Meta-analysis Study Group: Efficacy of omega-3 fatty acid supplements (eicosapentaenoic acid and docosahexaenoic acid) in the secondary prevention of cardiovascular disease: a meta-analysis of randomized, double-blind, placebo-controlled trials. Arch Intern Med 2012;172:686–694.

Background: Although previous randomized, double-blind, placebo-controlled trials reported the efficacy of omega-3 fatty acid supplements in the secondary prevention of cardiovascular disease (CVD), the evidence remains inconclusive. Using a meta-analysis, we investigated the efficacy of eicosapentaenoic acid and docosahexaenoic acid in the secondary prevention of CVD.

Methods: We searched PubMed, EMBASE, and the Cochrane Library in April 2011. Two of us independently reviewed and selected eligible randomized controlled trials.

Results: Of 1007 articles retrieved, 14 randomized, double-blind, placebo-controlled trials (involving 20 485 patients with a history of CVD) were included in the final analyses. Supplementation with omega-3 fatty acids did not reduce the risk of overall cardiovascular events (relative risk, 0.99; 95% CI, 0.89–1.09), all-cause mortality, sudden cardiac death, myocardial infarction, congestive heart failure, or transient ischemic attack and stroke. There was a small reduction in cardiovascular death (relative risk, 0.91; 95% CI, 0.84–0.99), which disappeared when we excluded a study with major methodological problems. Furthermore, no significant preventive effect was observed in subgroup analyses by the following: country location, inland or coastal geographic area, history of CVD, concomitant medication use, type of placebo material in the trial, methodological quality of the trial, duration of treatment, dosage of eicosapentaenoic acid or docosahexaenoic acid, or use of fish oil supplementation only as treatment.

Conclusion: Our meta-analysis showed insufficient evidence of a secondary preventive effect of omega-3 fatty acid supplements against overall cardiovascular events among patients with a history of cardiovascular disease.

Philipp M, Keune PM, Bostanov V, Hautzinger M, Kotchoubey B: Mindfulness-based cognitive therapy (MBCT), cognitive style, and the temporal dynamics of frontal EEG alpha asymmetry in recurrently depressed patients. Biol Psychol 2011;88:243–252.

Mindfulness-based cognitive therapy (MBCT), a meditation-based maintenance therapy, reduces the relapse risk in individuals suffering from major depressive disorder (MDD). However, only a few studies investigated the psychophysiological mechanisms underlying this protective effect. We examined effects of MBCT on trait rumination and mindfulness, as indicators of global cognitive style, as well as on residual depressive symptoms in a group of recurrently depressed patients ($n = 78$) in remission. Additionally, alpha asymmetry in resting-state electroencephalogram (EEG) was assessed. Alpha asymmetry has been found to be predictive of affective style and a pattern indicative of stronger relative right-hemispheric anterior cortical activity may represent a trait marker for the vulnerability to develop MDD.

In line with previous findings, residual depressive symptoms and trait rumination decreased, whereas trait mindfulness increased following MBCT, while no such changes took place in a wait-list control group. Mean values of alpha asymmetry, on the other hand, remained unaffected by training, and shifted systematically toward a pattern indicative of stronger relative right-hemispheric anterior cortical activity in the whole

sample. These findings provide further support for the protective effect of MBCT. In the examined patients who were at an extremely high risk for relapse, however, this effect did not manifest itself on a neurophysiological level in terms of alpha asymmetry, where a shift, putatively indicative of increased vulnerability, was observed.

Meeuwse EJ, Melis RJF, Van Der Aa GC, Golüke-Willems GA, De Leest BJ, Van Raak FH, Schölzel-Dorenbos CJ, Verheijen DC, Verhey FR, Visser MC, Wolfs CA, Adang EM, Olde Rikkert MG: Effectiveness of dementia follow-up care by memory clinics or general practitioners: randomised controlled trial. BMJ 2012;344:e3086.

Objective: To examine the effectiveness of post-diagnosis dementia treatment and coordination of care by memory clinics compared with general practitioners.

Design: Multicentre randomised controlled trial.

Setting: Nine memory clinics and 159 general practitioners in the Netherlands.

Participants: 175 patients with a new diagnosis of mild to moderate dementia living in the community and their informal caregivers.

Interventions: Usual care provided by memory clinic or general practitioner.

Main outcome measures: Caregiver rated quality of life of the patient measured with the quality of life in Alzheimer's disease instrument and self perceived burden of the informal caregiver measured with the sense of competence questionnaire (intention to treat analysis).

Results: The quality of life of the patients in the memory clinic group was 0.5 (95% confidence interval -0.7 to 1.6) points higher than in the general practitioner group. Caregivers' burden was 2.4 (-5.8 to 1.0) points lower in the memory clinic group than in the general practitioner group.

Conclusion: No evidence was found that memory clinics were more effective than general practitioners with regard to post-diagnosis treatment and coordination care for patients with dementia. Without further evidence on the effectiveness of these modalities, other arguments, such as cost minimisation, patients' preferences, or regional health service planning, can determine which type of dementia care is offered.

Sedlmeier P, Eberth J, Schwarz M, Zimmermann D, Haerig F, Jaeger S, Kunze S: The psychological effects of meditation: a meta-analysis. Psych Bull 2012; DOI:10.1037/a0028168.

In this meta-analysis, we give a comprehensive overview of the effects of meditation on psychological variables that can be extracted from empirical studies, concentrating on the effects of meditation on nonclinical groups of adult meditators. Mostly because of methodological problems,

almost 3/4 of an initially identified 595 studies had to be excluded. Most studies appear to have been conducted without sufficient theoretical background. To put the results into perspective, we briefly summarize the major theoretical approaches from both East and West. The 163 studies that allowed the calculation of effect sizes exhibited medium average effects ($r = .28$ for all studies and $r = .27$ for the $n = 125$ studies from reviewed journals), which cannot be explained by mere relaxation or cognitive restructuring effects. In general, results were strongest (medium to large) for changes in emotionality and relationship issues, less strong (about medium) for measures of attention, and weakest (small to medium) for more cognitive measures. However, specific findings varied across different approaches to meditation (transcendental meditation, mindfulness meditation, and other meditation techniques). Surprisingly, meditation experience only partially covaried with long-term impact on the variables examined. In general, the dependent variables used cover only some of the content areas about which predictions can be made from already existing theories about meditation; still, such predictions lack precision at present. We conclude that to arrive at a comprehensive understanding of why and how meditation works, emphasis should be placed on the development of more precise theories and measurement devices.

Herrschaft H, Nacu A, Likhachev S, Sholomov I, Hoerr R, Schlaefke S: Ginkgo biloba extract EGb 761® in dementia with neuropsychiatric features: a randomised, placebo-controlled trial to confirm the efficacy and safety of a daily dose of 240 mg. J Psychiatr Res 2012;46:716-723.

A multi-centre, double-blind, randomised, placebo-controlled, 24-week trial with 410 outpatients was conducted to demonstrate efficacy and safety of a 240 mg once-daily formulation of *Ginkgo biloba* extract EGb 761® in patients with mild to moderate dementia (Alzheimer's disease or vascular dementia) associated with neuropsychiatric symptoms. Patients scored 9 to 23 on the SKT cognitive battery, at least 6 on the Neuropsychiatric Inventory (NPI), with at least one of four key items rated at least 4. Primary outcomes were the changes from baseline to week 24 in the SKT and NPI total scores. The ADCS Clinical Global Impression of Change (ADCS-CGIC), Verbal Fluency Test, Activities of Daily Living International Scale (ADL-IS), DEMQOL-Proxy quality-of-life scale and 11-point box scales for tinnitus and dizziness were secondary outcome measures. Patients treated with EGb 761® ($n = 200$) improved by 2.2 ± 3.5 points (mean $\pm$ sd) on the SKT total score, whereas those receiving placebo ($n = 202$) changed only slightly by 0.3 ± 3.7 points. The NPI composite score improved by 4.6 ± 7.1 in the EGb 761®-treated group and by 2.1 ± 6.5 in the placebo group. Both drug-placebo comparisons were significant at $p < 0.001$. Patients treated with EGb 761® also showed a more favourable course in most of the secondary efficacy variables. In conclusion, treatment with EGb 761® at a once-daily dose of 240 mg was safe and resulted in a significant and clinically relevant improvement in cognition, psychopathology, functional measures and quality of life of patients and caregivers.